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THE ROLE OF THE EXPOSURE RATE IN ANGIOCARDIOGRAPHY

by

Carl Wegelius and *John Lind*

The development of the technique of angiocardiography has been characterized by continued efforts to increase the rate of serial exposures so as to obtain complete anatomic perception of the cavities of the heart and of the great vessels. Because of the toxicity of the contrast medium only a limited amount can be introduced into the circulation and the various regions are rendered opaque for only a relatively short period (depending on the speed of the circulation). We are generally satisfied if each separate heart chamber is adequately visualized in at least one of the films, thus permitting of an anatomic diagnosis. This type of angiocardiography we have termed 'anatomic' angiocardiography.

By this method, the heart and great vessels are seen anatomically with emphasis on morphologic and topographic features such as size, shape, position and intercommunications. It has given valuable results in diagnosis and guidance to the surgeon before operation. Standard angiocardiography of this type takes no account of the phase in the heart cycle in which the exposure is made, and the films are accepted as long as the filling is good enough to warrant anatomic conclusions. A further development of 'anatomic' angiocardiography is the so-called selective method, in which the contrast medium is injected under pressure through a catheter directly into the site of suspected pathologic changes. From this it follows that the method is limited to segments of the heart and cannot allow of considerations concerning cardiac activity as a whole. The momentarily increased and marked local pressure may also create

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From the Pediatric Clinic of Karolinska Institutet (Director: Prof. A. WALLGREN) and the Department of Cardiovascular Research, Norrtulls Hospital, Stockholm, Sweden.

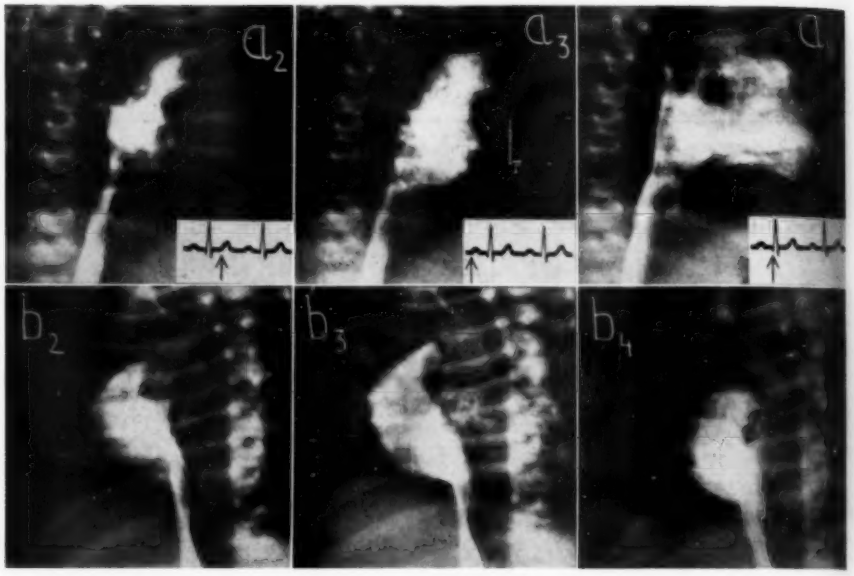


Fig. 1. *Dynamics of the right side of the heart. The morphologic changes as an expression of* Injection from below into vena malleolaris. Right (a_2—a_5 and a_7—a_8) and left (b_2—b_3 0.02 per second. Films synchronously

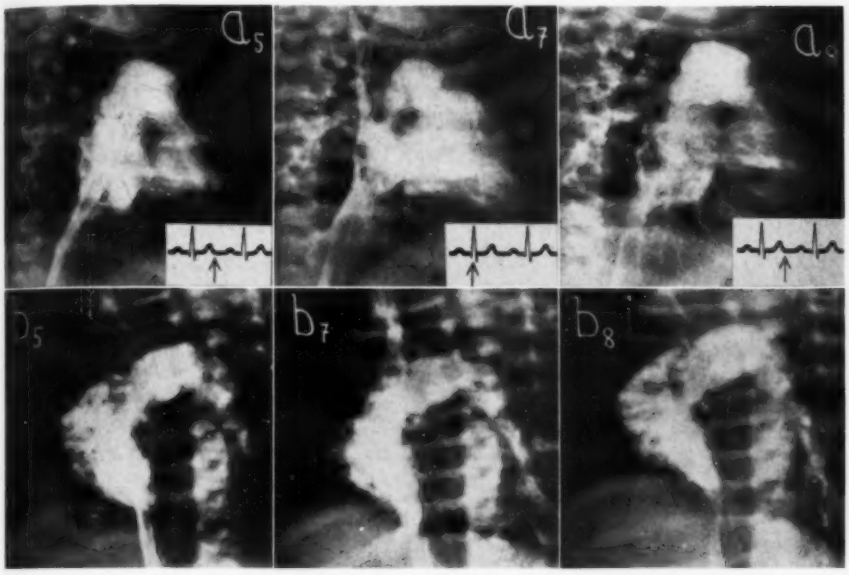
a_2b_2: The medium has just reached the heart. Right atrium in beginning of diastole. Auricular appendix clearly shown above the atrial lumen proper.

a_3b_3: End of the same diastole. Right atrium including the auricular appendix maximally filled, the whole cavity system fully distended. In b_3 small amounts of the medium pass through an atrial septal patency into the left atrium (patent foramen ovale).

a_4b_4: The following atrial systole. Right ventricle in diastole, well filled up to the pulmonary valves. The tricuspid valves, wide open, can be seen and evaluated. In atrial systole the auricular appendix has diminished to a small fraction of its diastolic size.

unphysiologic factors producing artificially influenced haemodynamic conditions.

If the speed of angiocardiographic serial recording is increased, more anatomic information may be obtained and in addition opportunities for the interpretation of the dynamic action of the heart may be presented. This has become possible in the last few years by technical developments which permit of such fast serial exposures that the extremes of one heart cycle *i. e.* maximal diastole and systole, as well as a sufficient number



heart work. Normal case (with the exception of an insignificant small patent foramen ovale).

and b_7—b_8) anterior oblique projections; rate 12 exposures per second, exposure time in pairs in two planes at right angles.

a_5b_5: End of the following ventricular systole. The pulmonary conus is now much more narrow and the pulmonary artery in comparison wide.

a_7b_7: End of the next atrial systole, when the atrium appears to be smallest. Pulmonary conus is again broad; the pulmonary artery has shrunk.

a_8b_8: Following ventricular systole with the ventricle in extreme contraction. The atrioventricular septum has moved a considerable distance toward the apex of the heart from its position during ventricular diastole (compare a_7 and a_8).

The dynamic effect of the emptying of the right ventricle seems to occur mainly in the left oblique diameter and can be best evaluated in the right oblique projection (the 'a' series). From a diastolic narrow-based triangular shape, the ventricle contracts in systole to a broad-based triangle at the heart base, indicating the systolic residual contents. In the left oblique projection (the 'b' series) the changes are limited to a decreased transverse diameter. The rôle of the movements of the atrioventricular septum has also been elucidated.

of intermediate phases may be radiographed in sequence. The dynamics of the heart may thus be subjected to critical study. The advantages of these methods have already been discussed in the literature by JANKER, BÖHME, ZDANSKY and WESTERMARK, as well as by ourselves.

The principal difference between the techniques which allow a physio-

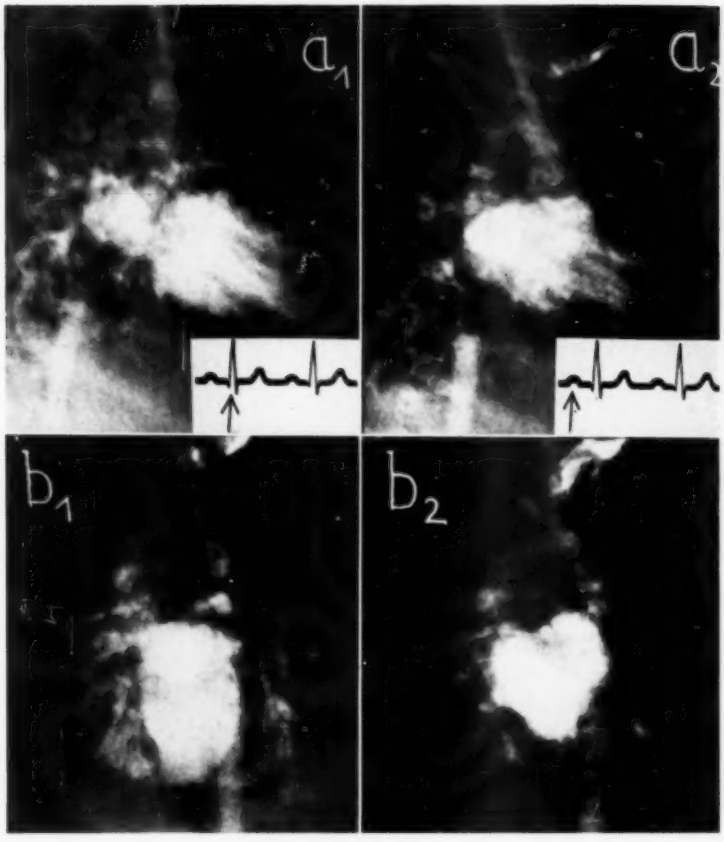


Fig. 2. *Dynamics of the left side of the heart. Normal case.*

Injection into the left median cubital vein. Right (a_1—a_2) and left (b_1—b_2) anterior oblique projections: rate and exposures as in Fig. 1.

a_1b_1: In atrial systole, the cavity of the left atrium is convex in every direction, almost spherical, and small in comparison to the broad, egg-shaped diastolic ventricular cavity.

a_2b_2: In the following ventricular systole, the left auricle contracts around its longitudinal axis, the cavity becoming almost cylindrical in shape. The aorta is widened with the arch lower and broader as a result of the systolic output (aortic pulsation).

The difference in the contraction dynamics of the left and right ventricle becomes evident. The rounded form of the left atrium is maintained almost the same in systole and diastole. This cavity is the only one in which the configuration seems to remain unchanged during contraction, which appears to occur more or less concentrically.

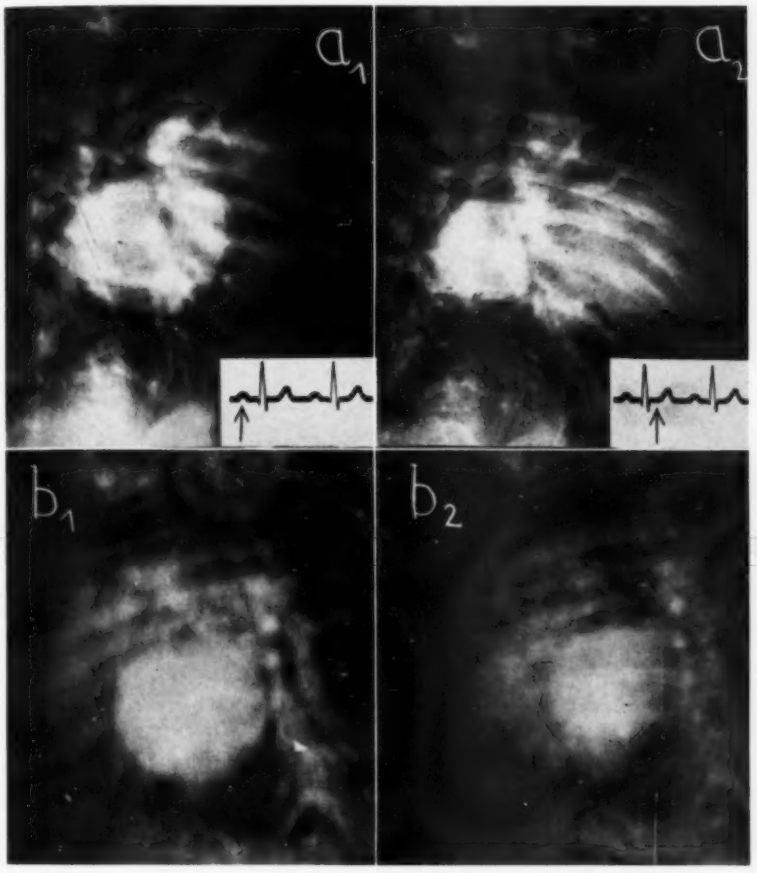


Fig. 3. *Angiocardiographic determination of the stroke volume of the left atrium.*
Injection into the right median cubital vein. Right (a_1—a_2) and left (b_1—b_2) anterior oblique projections.

a_1b_1: Left atrium in extreme diastole.

a_2b_2: $^1/_{12}$ of a second later. The left atrium is in systole and is now caught in the other extreme of the same heart cycle.

Due to the convex form of the left atrium in both projections, the volume of this cavity may be estimated approximately by calculation of its synchronous projection in two planes, using the same method as in determination of the heart volume. The difference between the diastolic and the systolic volume is equal to the stroke volume.

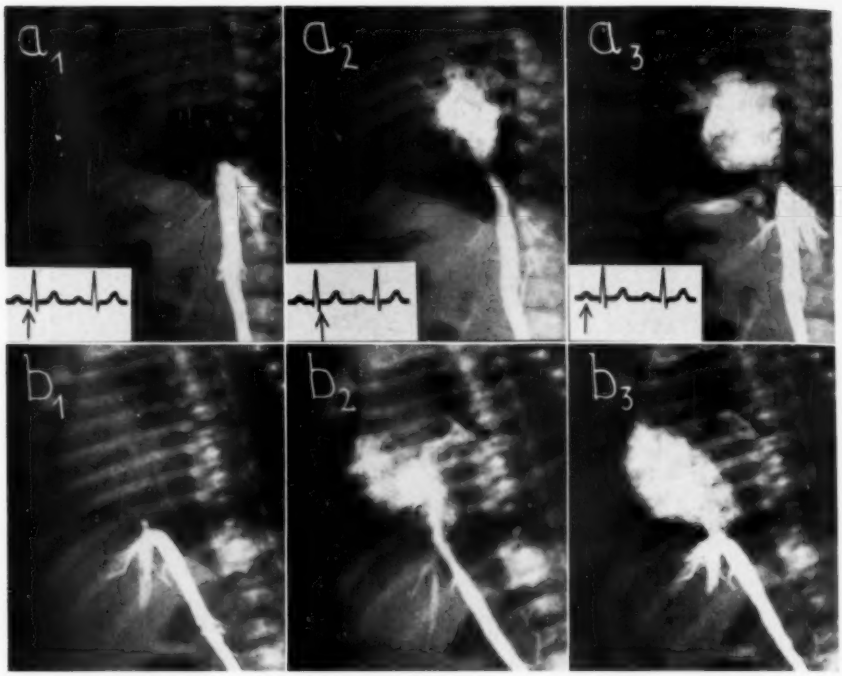


Fig. 4. *The venous inflow to the heart through the inferior vena cava. Normal case.* Injection from below. Right (a_1—a_3) and left (b_1—b_3) anterior oblique projections.

a_1b_1: The contrast medium has reached the right atrium, but is stopped during atrial systole at the orifice of the inferior vena cava, a part of the medium being diverted into the hepatic veins.

a_2b_2: Beginning of the following atrial diastole. An uninterrupted stream of medium is now passing into the right atrium, indicating that the passage is free. A small amount of medium is shunted over to the left atrium (patent foramen ovale).

a_3b_3: Right atrium at maximal size. Systole is just starting. Closure mechanism of the inferior caval vein is visualized as an abrupt difference in opacity at the margin of the atrial cavity.

The phenomenon of closure at the entrance of the inferior vena cava is repeated in the same phase of each heart cycle. The reflux of medium into the hepatic veins in relation to the cardiac cycle occurs in the same way. The medium is seen to be 'sucked' out again from these veins as soon as the flow into the heart is free.

logic assessment of the heart action and those restricted to anatomic perceptions lies in the rate of exposure.

In order to determine the minimal exposure rate it is necessary to

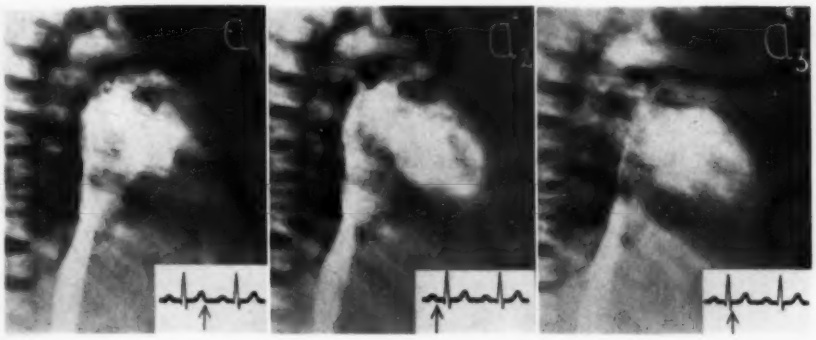


Fig. 5. *Transitory direct visualization of patent ductus* after intravenous injection.

Lateral projection.

a_1: Left auricle in maximal diastole; auricular appendage bulging; left ventricle in maximal systole.

a_2: Intermediate stage of auricular systole; auricle is emptying into the ventricle, which is half filled. The patent ductus arteriosus (verified by post mortem section) is 'caught' in this instant and clearly seen between the beginning of the descending limb of the aortic arch and the pulmonary artery.

a_3: In the film which follows and in which the left auricle and its appendage become more or less refilled, the patent ductus is no longer seen.

Visualization of the malformation is limited to a short period of the heart cycle, in which by coincidence the ductus is not only shown but contrast filled due to influx from the aorta.

know for how long each individual part of the heart is rendered opaque. As the opacity is related to the circulation rate, the determination of time is best expressed in terms of heart cycles. In this way, physiologically exact values, applicable at every frequency, are obtained, which would not be the case if the determination of time were expressed in seconds. It has been shown that the time taken to inject the contrast medium should not be longer than a duration of 3—4 heart cycles, the equivalent, we have found, of the pulmonary circulation time. With a slow rate of injection there is a danger that during the visualization of the right side of the heart some of the medium may pass through the lungs and appear on the left side. If this occurs, the various heart chambers cannot be satisfactorily projected separately as there is superimposition of the contrast-filled chambers. After two systolic contractions of the well-outlined right auricle, there is maximal filling of the right ventricle.

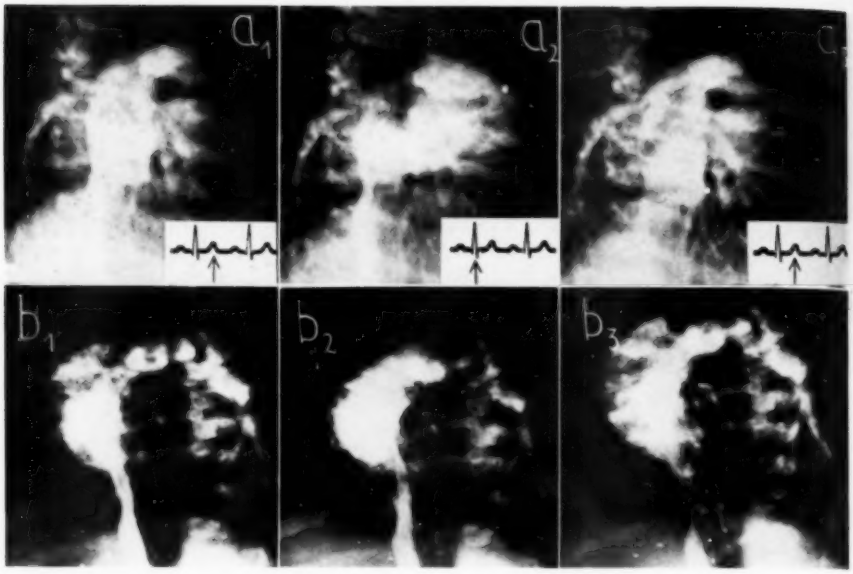


Fig. 6. *Indirect transitory sign of patent ductus arteriosus.*

Injection from below. Right (a_1—a_3) and left (b_1—b_3) anterior oblique projections.

a_1b_1: Right heart chambers well filled with contrast. Atrium in diastole, ventricle in systole. Pulmonary conus and artery clearly visualized. Increased vascular filling in the lungs.

a_2b_2: Atrial systole. Tricuspid valves wide open (a_2). Right ventricle filled in diastole. The stem and two main branches of the pulmonary artery are not visualized in this phase. The peripheral branches are clearly seen.

a_3b_3: During the following ventricular systole the whole pulmonary artery is again well filled.

The disappearance of contrast medium from the pulmonary artery, a sort of 'negative contrast', occurs as a result of intermittent shunts of non-opaque blood from the aorta through the patent ductus arteriosus. The evaluation of such functional phenomena, due to cardiac haemodynamics, requires this exact determination of their time relationship to the whole heart cycle. Otherwise they may lack diagnostic value.

Maximal filling of the left side of the heart and aorta normally follows 3—4 heart cycles later. The total time for the adequate filling of the left side of the heart and great vessels will be limited to 8—12 heart cycles from the time of arrival of the contrast medium in the right auricle. This corresponds to total times of 6—9 seconds for cardiac contrast visualization at a heart rate of 90 per minute, 4—6 sec. at a rate up to 120 per

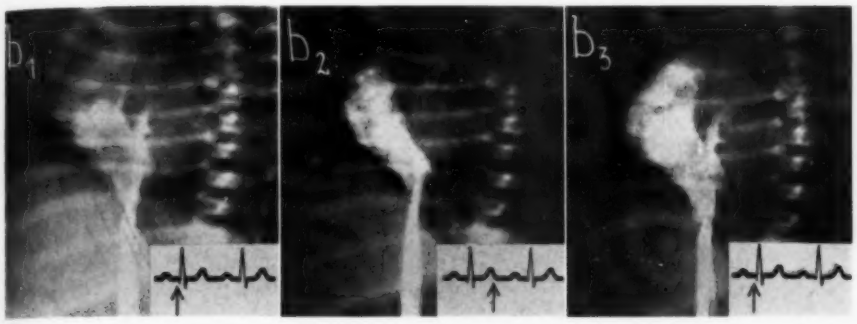


Fig. 7. *Atrial septal defect visualized only during atrial systole.*

Injection from below. Left anterior oblique projections; rate 12 exposures per second.

b_1: Atrial systole; right to left shunt into the left auricle through a small-sized atrial septal defect. The shunted medium is seen in the left auricle as a curved band of medium along the inner side of its medial wall.

b_2: In atrial diastole, no shunt into the left auricle is seen.

b_3: In the next atrial systole the same phenomenon is repeated as in b_1.

The shunt was confirmed by the fact that the whole left atrium showed considerable opacity in the films which followed, before any pulmonary circulation had occurred. The visualization of the atrial septal defect in this way is connected with a certain phase of the heart cycle.

minute and only 3 seconds at a rate of 180 per minute, the latter rate occurring in infants.

In 'anatomic' angiocardiography, the aim is fulfilled when each separate heart chamber is adequately filled and recorded in at least one film. Rapid blood flow and passage of contrast medium through the heart will demand certain minimum exposure rates in relationship to the heart rate. The following values are necessary to guarantee the recording of films showing complete optimal filling of both sides of the heart, the pulmonary system and the aorta:

heart rate	minimum exposure rata
90 per second	0.8 per second
120 per second	1.2 per second
180 per second	2.0 per second

In 'physiologic' angiocardiography in which not only one but several exposures of the same heart cycle are examined, the problem becomes more complicated as the component of motion has to be studied in addition and in relationship to the anatomic morphology. Every reproduction of motion must be adapted to the speed and excursions of an object. If the excursions are regular as in the heart, in which they swing be-

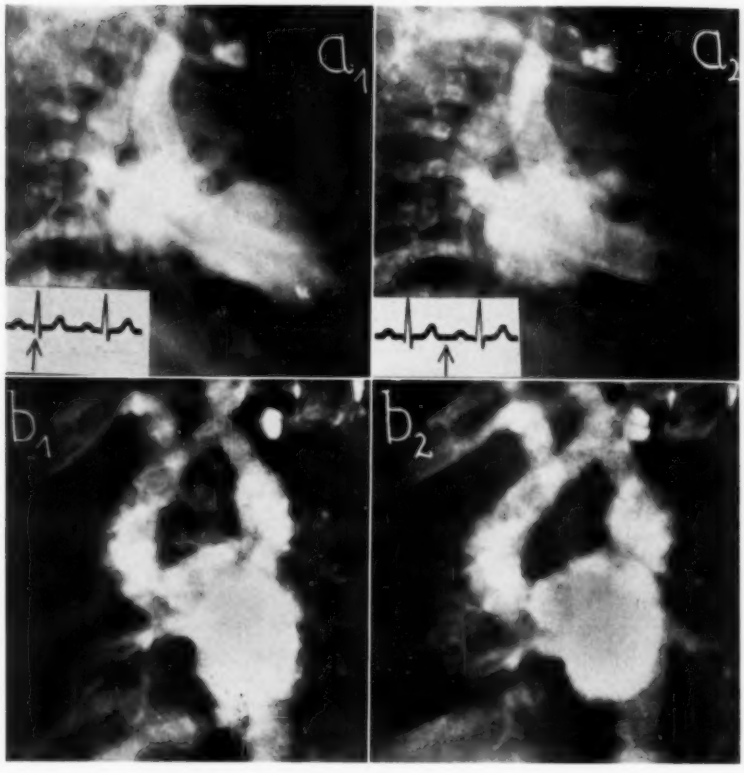


Fig. 8. *Elasticity in coarctation of the aorta.*

Injection into median cubital vein. Right anterior oblique (a_1 and a_2) and left anterior oblique (b_1 and b_2) projections.

a_1b_1: Ventricular diastole; moderate stenosis of aorta with poststenotic dilation clearly visualized.

a_2b_2: In ventricular systole the aorta, including the poststenotic segment is widened throughout. The narrowed section especially becomes broader and of almost normal caliber.

The serial recording gives valuable functional information. The coarctation is 'elastic' to a considerable degree and does not seem to hinder the passage to any extent.

tween the extremes of maximal systole and diastole, they will be fixed by these extremes. A sufficient number of intermediate phases between the two extremes must also be reproduced in order to demonstrate the relationship of the dynamics to the course and duration of the morphologic

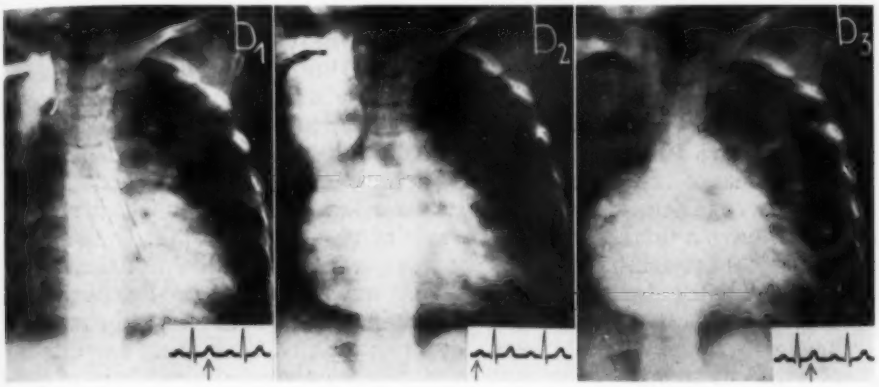


Fig. 9. *Rapid transitory visualization of malformation of the superior vena cava.*
Injection into median cubital vein. A—p projection: exposure time 0.08 sec.

b_1: Commencing contrast filling of superior vena cava.

b_2: 0.08 sec. later. An aneurysmal dilation of the superior vena cava is visualized.

b_3: 0.32 sec. after b_2. The medium is completely emptied from the superior vena cava, the malformation no longer being seen.

The timed serial recording shows that the entire opaque rendering of the malformation lasted less than 0.4 sec. Diagnostic visualization might thus have failed even with an angiocardiographic recording at 0.5 sec. intervals, *i. e.* an exposure rate of 2 exposures per second.

changes. Recognizing the importance of angiocardiography for the early diagnosis of congenital heart defects in infants, the demands of dynamic recording must be fulfilled even at the high heart rates common in the first years of life. If these requirements are met, the exposure rate will certainly suffice to record the slower heart rates of older children and of adults.

In angiocardiography in infants, it is necessary to deal with heart rates of 120 to 180 beats per minute. A rate of 180 means three complete heart cycles per second. For practical purposes, the ratio between auricular systole and diastole at this frequency may be assumed to be 1 : 2 and between ventricular systole and diastole about 2 : 1. It will therefore require at least three exposures per heart cycle to catch the auricle and the ventricle both in systole and in diastole. This means that with a frequency of 3 heart cycles per second there must be at least 9 exposures per second. At this speed one film is obtained of each auricular systole and ventricular diastole and two films of each auricular diastole and ventricular systole. It was previously stated that even in an adequate

angiocardiography one cannot count on completely satisfactory filling of the different cavities for more than 3 to 6 heart cycles, that is, for only 1 to 2 seconds at a heart rate of between 180 and 90 per minute. At a rate of 9 exposures per second this would mean not more than 3 to 5 films in systole and 6 to 9 films in diastole. A safety margin of 1 to 3 films per second above the minimum demand of 9 exposures per second gives a greater chance of properly assessing the dynamics of the complete heart cycle. In consideration of these facts we believe that in infants it is necessary to have a minimum exposure rate of 10—12 per second. With heart rates of 90 per minute, 5—6 exposures per second will be sufficient and between these extreme values a suitable exposure rate may be chosen.

In transitory phenomena such as rapid variations in size and shape of the heart chambers, the length of the exposure time is an important factor. It must be short enough to represent only a definite phase of the heart cycle on the film. As maximum systole and diastole last for about 20 per cent of the total phase duration, the longest exposure time that can be allowed will be only 0.02 second with a heart rate of 180 per second. With slower heart rates, the exposure time may be lengthened to 0.03 or 0.04 seconds.

In order to assess the dynamic action of the heart it is necessary to show each heart chamber in extreme systole and diastole as well as, and most importantly, in some of the intermediate phases. As we already know from kymography, the heart movements are not uniform in speed and amplitude. From calculations of proportional periods in the heart cycle of maximum systole and diastole, these demands are fulfilled at all heart frequencies in question at the exposure rates of 10—12 exp./sec., used in our angiocardiographic technique.

By combining the films with a synchronous ECG with automatic exposure marks obtained off one of the standard leads, direct legible correlation between the intervals of the exposures and the phase of the heart cycle may be obtained. It is thus possible to time the separate films in relation to the heart cycle and further, by following a sequence or other combination of films, to determine the nature of the morphologic changes which have occurred.

For the assessment of the applicability of these theoretical conclusions it is necessary to consider the character and significance of the diagnostic problems. The question is best considered if firstly we determine what diagnostic conclusions are generally unobtainable without the aid of fast 'dynamic' or 'physiologic' angiocardiography (group A). Secondly, we can calculate the probability of catching certain significant signs only occasionally observed with the slower method (group B).

Group A, principally physiologic observations, includes all considerations on the dynamic action of the heart. This is most easily illustrated

with a few typical examples (Figs. 1—4). The conclusions reached are discussed in the legend accompanying each figure. By studying the dynamics of the heart, valuable physiologic phenomena may obviously be recorded and utilized for diagnostic purposes. The most important achievement gained seems to us to be the opportunity of defining the dividing line between the normal and the pathologic in the following groups of problems:

1. The mechanism of contraction of the separate heart chambers as well as of the heart as a whole.

2. The passage of the contrast medium through the heart and the great vessels with special reference to course, velocity, distributions, regurgitation etc.

3. The haemodynamic effect of the work of the heart in the light of the correlated aspects 1 and 2.

It may be stressed that all 'physiologic' observations of this character are based on 'anatomic' considerations obtained by the recording of the morphologic changes the heart and its cavities undergo as a visible expression of its work, *i. e.* the dynamics of the heart. 'Dynamic' and 'anatomic' angiocardiographic recordings are thus not opposites. The former may be regarded as a perfection of the latter and affording new 'physiologic' aspects due and in addition to improved anatomic concepts.

Group B includes 'anatomic' signs which, due to their transitory nature, will only occasionally be visualized with the slower exposure rate, but which are certainly recorded with the faster method. A few examples are shown in Figs. 5—9. They include cases of atrial septal defect, patent ductus arteriosus and coarctation of the aorta. It will be seen from the illustrations and legends that direct visualization of the two forms of malformations may only be caught radiographically during

	Direct visualization in comparison with the whole heart cycle	Chances of visualizing with exposure rate of 1 per sec. at different heart frequencies. *Heart frequencies:* 90 per min.	120 per min.	180 per min.
1. Patent ductus arteriosus (ductus itself)....	1 : 2	3 : 8	3 : 11	3 : 16
2. Atrial septal defect (defect itself).....	1 : 3	1 : 4	1 : 5.5	1 : 8
3. Elasticity in coarctation of the aorta.....	1 : 7 max. calib.	1 : 9.5	1 : 12	1 : 19
(The determination requires the recording of extremes of caliber variations in both systole and diastole. As both extremes have to be caught, it is necessary to calculate on the basis of the less favourable chances, *i. e.* the figures for max. caliber).	1 : 4 min. calib.	3 : 16	3 : 22	3 : 32

a part of the heart cycle and may thus escape diagnosis. In coarctation of the aorta, the elasticity of the narrowed aortic wall plays such an important rôle, that its determination may be of considerable surgical value.

This comparison shows that the theoretical chances of visualizing and recording these malformations with the standard exposure rate of 1 per second are small at the lower heart rates, and hardly possible at the faster rates. This probably explains why they are so seldom recognized directly in ordinary angiocardiography. In such cases, one was formerly forced to make a diagnosis on indirect signs — such as abnormal refilling in the opposite direction to the normal blood flow. Neither the anatomic data regarding size, shape and position could be determined, nor was it possible to judge the degree of any patho-physiologic defect.

Discussion

Angiocardiography, for the patient, is still a troublesome examination and not without risks. Thus, before carrying out such a procedure, one has to evaluate most carefully the probable diagnostic result. If it is possible to amplify the diagnosis by technical improvements without injury to the patient, these are worth considering. An increased rate of exposure is thus a true step forward.

From our analysis it would appear that the present standard method with a slow rate of exposure will, as a rule, offer satisfactory anatomic information on the inner morphology of the heart and the great vessels, provided there are no malformations, demonstrable only as rapid transitory phenomena, present. These will be shown only by chance, and must be evaluated from indirect signs. This is unfortunate, as their considerable clinical importance often implies direct visualization. The factor is especially important, bearing in mind the rapid development of heart surgery.

Fast angiocardiography will increase the possibilities of registering anomalies, and will also enable general morphologic studies to be carried out. In addition, the mode of action of the heart in normal and pathologic conditions will be open for roentgenologic analysis and critical evaluation. The regular use of this new diagnostic method may be expected to fulfill a definite rôle.

SUMMARY

The influence of the exposure rate in angiocardiography is generally discussed. The relative merits of the 'anatomic' and 'dynamic' methods of examination are pointed out. The latter, incorporating simultaneous electrocardiography and automatic exposure marking, correlates all the information given by the former with the more physiologic aspects of the heart mechanism.

ZUSAMMENFASSUNG

Der Einfluss der Exponierungsdaten bei der Angiokardiographie wird allgemein diskutiert. Die relativen Vorteile der „anatomischen" und „dynamischen" Untersuchungsmethoden werden hervorgehoben. Die Letztere, bei der gleichzeitig die Elektrokardiographie und eine automatische Exponierungsanzeige stattfindet, vergleicht alle Informationen der erstgenannten Methode mit den mehr physiologischen Aspekten des Herzmechanismus.

RÉSUMÉ

Les auteurs examinent d'une façon générale l'influence de la cadence de prise des clichés en angiocardiographie. Ils font ressortir les avantages respectifs des méthodes d'examen «anatomique» et «dynamique». Celle-ci comprenant l'électrocardiographie simultanée et l'inscription automatique de la prise des clichés, relie tous les renseignements fournis par la première à des aspects plus physiologiques du mécanisme du cœur.

REFERENCES

Böhme, W.: Kymographische und röntgenkinematographische Untersuchungen der Herzfunktion. Röntgenbl. 3 (1950), 288; 4 (1951), 12.

Fredzell, G., Lind, J., Ohlson, E., and Wegelius, C.: Direct serial roentgenography in two planes simultaneously at 0.08 second intervals. Am. J. Roentgenol. 63 (1950), 548.

Janker, R.: Apparatur und Technik der Röntgenkinematographie zur Darstellung der Herzbinnenräume und der grossen Gefässe. (Angiokardio-Kinematographie.) Fortschr. Röntgenstr. 72 (1950), 513.

Keyes, T. F., Wegelius, C. and Lind, J.: The diagnostic value of dynamic studies in angiocardiography. Evaluation of new rapid technique. J. Thorac. Surg. 21 (1951), 164.

Lind, J., Wegelius, C., Fredzell, G. and Wasser, E.: Direct angiocardiography: experiences with 10 exposures per second. J. Fac. Radiol. 1 (1949), 87.

Lind, J. and Wegelius, C.: New trends in angiocardiography. Med. Illust. 4 (1950), 135.

Lind, J. and Wegelius, C.: Angiocardiographic studies in children. Advances in Ped. 5 (1952), 154.

Wegelius, C. and Lind, J.: The dynamics of the heart: observations by angiocardiography. J. Fac. Radiol. 3 (1952), 193.

Wegelius, C. and Lind, J.: Diagnostic evaluation of the heart dynamics by angiocardiography. Mod. Trends in Diagn. Radiol. (in print).

Westermark, N.: Roentgen studies of the lungs and heart. Minnesota Univ. Press (1948).

Zdansky, E.: Zur Röntgenologie der Dynamik des Herzens. Fortschr. Röntgenstr. 75 (1951), 179.

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ARTEFACTS IN AUTORADIOGRAPHY

by

Erik Odeblad

In recent years autoradiography has become widely used in the study of many medical and biologic problems. Due to the fact that the method demands a sensitive medium, the photographic emulsion, artefacts in autoradiographic films may easily occur and lead to erroneous conclusions. The scope of the present paper is to draw attention to such artefacts and discuss how they may be reduced or avoided. The contribution is founded on a material of about ten thousand autoradiographic negatives utilizing the radioisotopes P^{32}, S^{35}, C^{14}, Se^{75}, Cd^{115} and those in the thorium series, all produced with different autoradiographic techniques. About one half of these films has shown minor or major artefacts.

In autoradiographic work, variations in density of a statistical nature, as well as systematic errors in density may occur. These are due to variations and technical errors in the employment of the radioisotope, in the thickness of the emulsion, in the histologic section, and so on. However, with an artefact we mean a more qualitative disturbance which cannot be adequately expressed in terms of a statistical or systematic error. It is thus important that care be taken to recognize and prevent its occurrence.

Artefacts in autoradiography have been summarized previously by YAGODA (1949), by DONIACH and PELC (1950) who worked with the stripping film technique, by HERZ (1951) and by ODEBLAD (1952 (25)) employing roentgen film.

Principles of Autoradiography

Before the causes and prevention of artefacts can be understood, the fundamentals of autoradiographic technique must first be appreciated.

Lecture delivered at a colloquium on autoradiography at Sabbatsberg Hospital. Stockholm, on the 15th May, 1952; submitted for publication, Oct. 10, 1952.

In autoradiography a histologic section containing a radioisotope is brought in contact with a photographic emulsion, and due to the inherent radiation a representation of the radioisotope indicating its distribution within the section, is obtained. As shown in Fig. 1, three components are involved in the autoradiographic mechanism: (1) the histologic section containing the radioisotope, (2) the radiation and (3) the emulsion. The properties, handling and interaction of these components may give rise to artefacts in the final autoradiographic film.

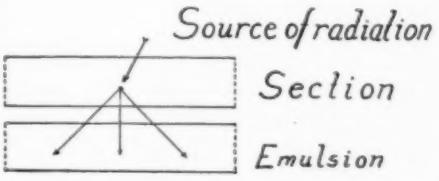


Fig. 1. The principle of the autoradiography exposure.

Several methods of autoradiography are in use: (1) The most simple technique, originally used by LACASSAGNE and LATTES (1924) is to bring a histologic preparation in contact with a sensitive film (usually roentgen film) and then to separate both and develop the latter. This technique is known as the separation technique and has been modified and amplified by many workers. On the other hand, there are several methods employing a more permanent contact between emulsion and section, known as 'integral techniques'. (2) One of these methods, introduced by BÉLANGER and LEBLOND (1946) is to paint the emulsion directly on to the section. The emulsion and the section are then in close contact during the photographic and histologic processing. This is termed coated autoradiography. (3) In the stripping film technique, a thin emulsion on a gelatin or celluloid base is floated on water with its sensitive side downwards and is then lifted from the surface by raising a slide with the section underneath it. This technique was originally developed by PELC (1947). (4) EVANS (1947) and ENDICOTT and YAGODA (1947) mounted the histologic section directly on the photographic plate. This type of mounting was further advanced when (5) BOYD and LEVY (1950) began to use nuclear emulsion autoradiography for nuclear and atomic research; the emulsion recorded the tracks of the individual beta particles emitted from the nuclei of radioactive atoms.

These five methods have been used by the author. Other types of autoradiography have been developed also but are not included in this contribution; they are (6) the inverted autograph technique of BÉLANGER (1950), (7) the wet process technique of GOMBERG (1951) and (8) focussed autoradiography of MARTON and ABELSON (1947).

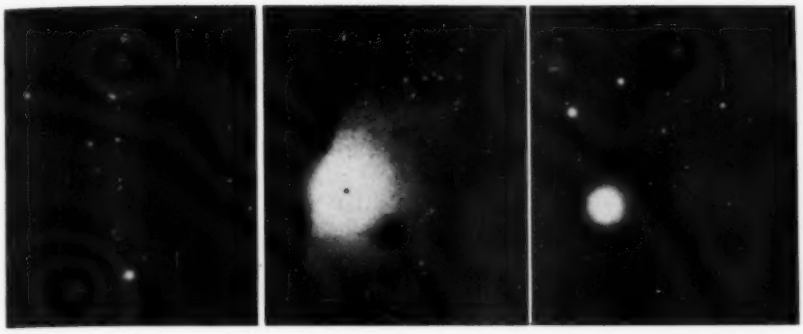
Artefacts Due to the Administration of the Radioisotope

The amount of carrier employed with the radioisotope must be sufficiently small to avoid unphysiologic reaction. This is of importance in the study of the thyroid with radioiodine or of bone with radiophosphorus, as pointed out by LEBLOND, WILKINSON, BÉLANGER and ROBICHON (1950). In certain cases, as in steroid investigations with C^{14}-autoradiography, the large number of radioisotope atoms causes a natural limitation of the minimum amount of carrier (LEBLOND, 1951) due to the long half-life and the large molecules. In other cases of (n, γ)-reactions, the neutron flux in the atomic pile cannot activate the element more than a certain degree because of the small cross-section, as in Se^{75}-autoradiography (JORPES, ODEBLAD and BOSTRÖM, 1953). On the other hand, carrier-free solutions must be used with great caution because they show unique reactions, such as co-precipitation, formation of colloidal aggregates and adsorption, as pointed out by BONNER and KAHN (1951). A carefully selected amount of carrier often gives the most appropriate results.

The treatment of the animal with the radioactive isotope may give rise to artefacts. After intravenous injection of radioisotopes, colloidal aggregates may be rapidly incorporated in the reticulo-endothelial system and disturb the images of certain organs, notably the liver, spleen and lungs. This type of artefact and its prevention has been carefully studied by LAMERTON and HARRISS (1952). Figs. 2 a and b illustrate the effect of colloidal aggregates of P^{32} in the solution for injection. HARRISON and RAYMOND (1952) and ODEBLAD (1952 (25)) have advised certain technical procedures, such as cleaning the bottles with glass powder or with carrier solution, that prevent the formation of colloidal aggregates. Radiocolloids, after subcutaneous injection, accumulate in the regional lymph glands and produce 'spotty' autoradiographs. After intraperitoneal injection, colloidal aggregates may be found, especially on the peritoneal surface of abdominal organs (Fig. 2 c).

The radioisotope sometimes contains contaminations of other isotopes which have originated from the neutron irradiation in the atomic pile. It is therefore necessary to have access to information regarding the purity of the radioisotope used; small amounts of $Na_2S^{35}O_4$ in $Na_2HP^{32}O_4$-autoradiography may accumulate in cartilage and disturb the picture.

The radiation from the isotope may cause functional or structural damage, which highly complicates the interpretation and significance of the results of the autoradiographic investigation. HEVESY (1948, p. 330) and HOLMES (1949) have shown that nucleic acid re-synthesis is depressed by radiation; this is of special importance in autoradiography with P^{32}, especially in the stripping film technique in which large amounts



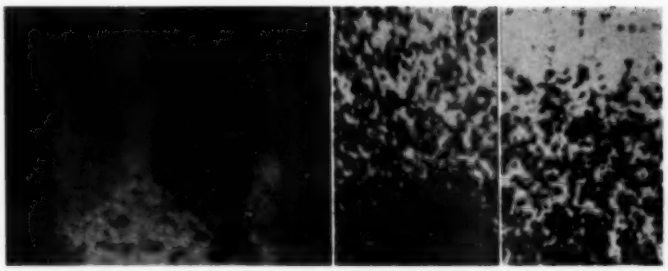
a. b. c.

Fig. 2. Heterogeneous distribution of P^{32} (white areas) due to the presence of colloidal particles containing P^{32} in the solutions for injection. a. Lung. × 5. b. Ovary. An intense point source of radiation has caused solarization (the black point in the centre of the light area). × 7. c. Autoradiograph of the uterus of a mouse which received an intraperitoneal injection of radiophosphate containing colloidal particles, and which have accumulated on the peritoneum. × 5.

of radioisotope are required. The question has been studied by PELC (1951) who by theoretical reasoning gave the rather low figure of 1 rep/day for C^{14} for an exposure over a period of 40 days on fine-grain stripping film. In a work on the highly radiosensitive granulosal tissue of the ovary of mice, ODEBLAD (1952 (26)) found that considerable histologic damage occurred in doses exceeding 3 μC/g of P^{32}-labelled phosphate. Such high dosage was found necessary in order to obtain satisfactory autoradiographic images on fine-grain stripping film (AMINOFF, MAGNUSSON and ODEBLAD, 1952). Radiation-induced changes in autoradiography, may be minimised by concomitant premedication with sulfhydryls (*e. g.* 2,3-dimercaptopropanol, ODEBLAD, 1952 (27)). Because certain sulfhydryls (mercaptanes) may interfere with the photographic processes, the integral techniques of autoradiography must then be used with great caution.

Artefacts Due to Histologic Treatment

Histologic treatment has the aim of preserving the histologic structure and of fixing the radioactive atoms and preventing their diffusion. A considerable equalization of differences in density is otherwise obtained or the isotope is lost in the fixing and other solutions. This problem has been studied by WINTERINGHAM, HARRISON and HAMMOND (1951) for water-soluble tracers.

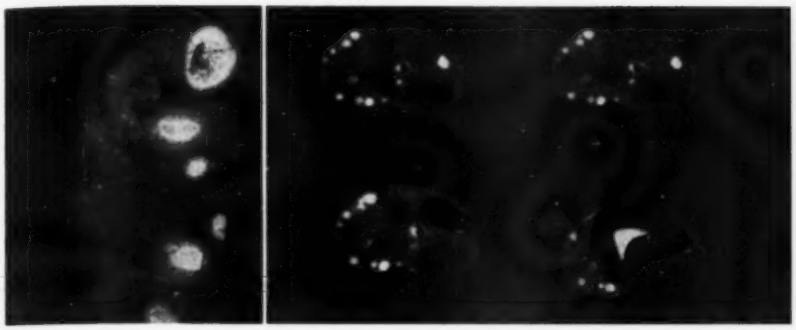


a. b. c.

Fig. 3. Inhibition of development due to diffusion of trichloracetic acid from the section. a. from a corpus luteum (P^{32}). The dark spots are the areas with inhibited development. ×10. b. Margins of inhibited development; also shows that the silver grains (light) are very small at the site of the inhibition (down). ×320. c. Illustrates demarcation between high (up) and low (down) exposure. The silver grains, all of same size, are more scanty in the weakly exposed area. × 320.

In order to obtain as high a resolution as possible, the section must be kept in very close contact with the emulsion. This intimate contact is one of the most important sources of artefacts because chemical interference due to the diffusion of substances from the section into the emulsion is considerably facilitated. The diffusion may occur during the wet processing in the integral techniques which demand permanent contact between emulsion and section. BOYD and BOARD (1949) have for example observed local fogging around bone marrow cells in the NTB nuclear emulsion. The histologic treatment is therefore of great importance for the quality of the image. The tissue may contain reducing substances which may cause the formation of a latent image, or oxidizers which may destroy a latent image in the photographic emulsion. The addition of formalin, mercury chloride or other chemical agents to the fixing solution may cause subsequent interaction with the emulsion. Alkaline substances increase and acid substances retard the rate of development. Figs. 3 a—c illustrate how trichloracetic acid used as a fixative may inhibit development. When stained sections are brought in contact with photographic emulsions (LEBLOND, PERCIVAL and GROSS, 1948) it is especially important to recognize the question of chemical influence on the emulsion. Chemical interferences have been carefully discussed by YAGODA (1949, p. 6); they may be prevented by interposing a thin layer of material (Kodak Film Lacquer, Celloidin etc.) between emulsion and section.

Other artefacts in the histologic section are major or minor structural displacements due to shrinkage during fixing. Such changes cause dis-



a. b.

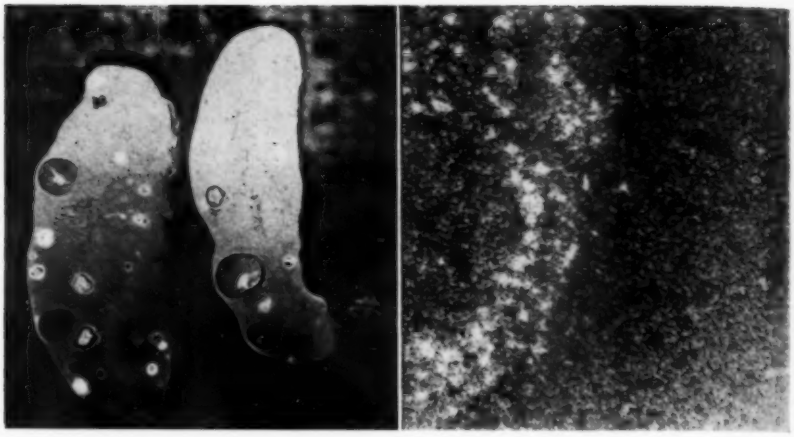
Fig. 4. a. Agglutination of radioactive phospholipides (P^{32}) in microincineration. × 12. b. Inhibition of development due to retained paraffin on the surface of film. Four autoradiographs with S^{35} of ovaries from guinea pigs. One (lower right) is masked by the artefact. Development completely inhibited over large area (dark), in the centre of which is a white spot caused by silver bromide, unaffected by fixing. × 5.

tortion of the autoradiographic picture, and possible misinterpretation. Thus, fissures in the section are accompanied by translucent stripes in the negative. A similar artefact has been described by PALM (1948, p. 82). In the recent approach to high resolution autoradiography by the mechanical enlargement of histologic sections (FINK, 1951), fissures and other mechanical artefacts were found to be very important. The knife of the microtome must be smooth and not cause scratches and fissures in the section. In addition, careful mounting of the histologic section is of great importance, because any wrinkling produces distortions in density. The exposure is most intense from the edges of the wrinkles due to the inverse square law; pressure effects causing impairment of resolution may also occur. It has proved necessary to deparaffinize the section before use, otherwise paraffin adheres to the film surface and prevents development and fixation (Fig. 4 b).

If micro-incineration be carried out, molten lipids in frozen sections may agglutinate in droplets as shown in Fig. 4 a.

Artefacts Present in the Emulsion before Exposure

During the manufacture of an emulsion, the sensitivity and thickness are determined. Considerable variations may occur in these factors (ODEBLAD, 1952 (25)), leading to variations in the autoradiographic density. Primary errors due to other flaws in the manufacture may also occur. If the emulsion has been bent or subjected to other mechanical trauma,



a. b.

Fig. 5. a. Autoradiographs of rabbit ovaries subjected to uneven pressure (most marked at top where photographic density is high). Outside the ovaries pressure effects have also occurred. Effects of dust between the slide and the film present. × 7. b. Autoradiograph of cervix uteri of mouse injected with S^{35} (left). The radiosulphur has entered into mast cells, visible as bright spots. (Right) fog area also shows bright spots, not, however, due to mast cells but to the irregular (Poisson) distribution of grains. × 40.

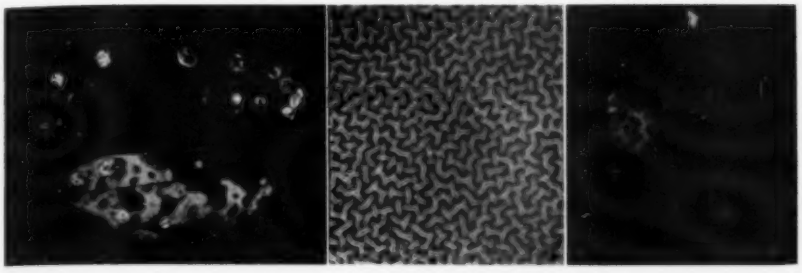
false densities may be produced. As the occurrence of such artefacts cannot be controlled, great caution must be taken in the analysis. Vaporized formaldehyde, which is always present in histologic laboratories, destroys the gelatin of the emulsion, the photographic material must consequently be stored in a separate department.

Certain emulsions, especially the nuclear emulsions, undergo ageing and rapidly become unserviceable.

Artefacts Occurring during the Exposure

Pressure applied during the autoradiographic exposure in order to improve contact may also cause special artefacts (pressure effects). Pressure renders the silver halide crystals developable and thus causes increased density. Pressure artefacts were discussed by Doniach and Pelc (1950), Yagoda (1949, p. 14) and by Odeblad (1952 (25) p. 25); they may occur at the edges of wrinkles, near the margins of the section or other points of high pressure. Pressure artefacts are illustrated in Figs. 5 a and 6 a.

Spark-induced development (Fig. 7 a) is due to the occurrence of



a. b. c.

Fig. 6. a. Autoradiographs with S^{35} of rabbit ovaries. Irregular bright areas due to pressure effects (bottom). × 5. b. & c. Reticulation. b. film given uniform light exposure. c. autoradiographic of mouse ovary with P^{32} completely spoiled by reticulation. × 7.

friction-induced static electricity on the film and the slide during manipulations before exposure. Sparks are frequent in the use of methacrylate slides. They are avoided by careful handling; it is particularly essential to avoid friction.

Luminescent interferences may be due to the occurrence of 'Bremsstrahlung', annihilation radiation, fluorescence or Cerenkov radiation as discussed by ODEBLAD (1952 (25 p. 56 and 70)) and by YAGODA (1949, p. 8 and 223). They may partly be avoided by a black foil interposed between section and emulsion.

Pseudo-photographic effects (due to chemical interaction) have already been pointed out. It is necessary to make control exposures with sections from the same tissue without radioisotope in order to see whether the section produces blackening. It is also useful to expose such a film to light and to ascertain whether development is inhibited.

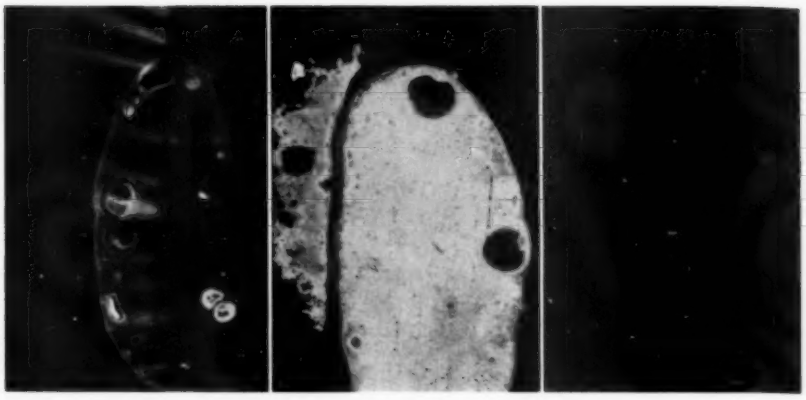
It is also essential to protect the region of exposure from interference from other histologic sections containing radioisotopes, a precaution sometimes overlooked.

The time of exposure is of importance especially in fine-grain emulsions, such as stripping film and nuclear emulsions, because of fading of the latent image (YAGODA, 1949, p. 291).

The humidity during the exposure must not be too high; it increases fading and, due to swelling of the gelatin, disturbs the geometrical interrelations between the emulsion and sections.

Artefacts Occurring during Photographic Processing

Due to streaming, uneven temperature, etc., development may be impaired, leading to streaks and generally 'spotty' effects.



a. b. c.

Fig. 7. a. Autoradiograph of rabbit ovary with S^{35}. Distortion due to static electricity also visible outside the autoradiograph. × 7. b. Irregular surface precipitation of silver in autoradiograph with P^{32} of rabbit ovary. × 7. c. Digital pressure causing inhibition of development. × 7.

Another type of uneven development, leading to distortions in density is known as development effects. They are well known in general photographic work and are described in full in the ordinary photographic handbooks (*e. g.* MEES, 1948, Chapter XXI, JAMES and HIGGINS, 1948, Chapter 13). Development effects occur near the lines of demarcation between high and low density and cause exaggeration of the differences in density or displacement of the spots of maximum density. As pointed out by ODEBLAD (1952, 25, p. 60) they are avoided by the use of slow-acting developers and low density levels.

Surface precipitation of silver (Fig. 7 b) occurs if the fixing bath contains too large an amount of silver; dichroitic fog (colloidal silver) in the interior parts of the emulsion may then also occur. The surface-precipitated silver may be removed by very short treatment in Farmer's solution, followed by rinsing in acetic acid, washing in water and then drying. The procedure must be performed rapidly (within a few seconds) in order not to damage the autoradiographic picture. Dichroitic fog cannot be removed.

Due to the very high vulnerability of the wet emulsion, the occurrence of mechanical injuries is a common event during the photographic processing. They are prevented by careful manipulation. If manifest, they cannot be repaired. Gelatin effects occur as local contractions caused by the use of certain developers. Pyrogallol produces contractions around

spots of high density, while hydroquinone does not. Due to shrinkage of the emulsion relatively to the base, ruptures of the former may occur, especially in the case of any tanning action of the developer and fixing bath. Reticulation (Fig. 6 b and c) is a special change in the gelatin and was thoroughly described by DONIACH and PELC (1950) who believed that it was due to sudden changes in temperature during processing. Successive treatment of the gelatin with swelling and dehydrating reagents also produces reticulation (MEES, 1948, p. 85).

In the drying of the emulsion, uneven moisture in the gelatin produces migration of silver grains (MEES, 1948, p. 86), which may cause distortions of the image. This phenomenon is easily avoided in the separation technique by the use of 'wetting agents' in the photographing processing baths. In the integral techniques uneven water retention in the section is probable and may initiate migration of silver grains.

Miscellaneous Artefacts

The graininess of the photographic emulsion implies an important source of error. There is a random distribution of grains, following the Poisson distribution law

$$p(n) = \frac{a^n \exp(-a)}{n!}$$

where $p(n)$ is the probability of finding n grains in a given volume of the emulsion and a is the mean number of grains in such a volume.

If we consider the fog in an area of $8 \cdot 8\ \mu^2$ in Gevaert Dentus Rapid film (17 μ thick), there are 5 fog grains as a mean in such a volume. The probability of finding a square with this number of grains is 0.18 and the probability of encountering a square with the double density (10 grains) is as high as 0.02. This means that the relatively common appearance of dense 'spots' may be misinterpreted as autoradiographs of point sources of radiation (See Fig. 5 b).

Dirt may originate from finger pressure and from impurities in the photographic processing baths; it may, however, have a complex origin. Digital pressure may inhibit development (Fig. 7 c). Dirt may often be removed by washing the developed, fixed and dried film in chloroform. Dust that has accumulated on the film before the exposure, increases the interspace between the emulsion and section (as is clearly shown in Fig. 5 a) and impairs resolution. It is therefore most essential to avoid dirt and dust by absolute cleanliness in the handling of the autoradiographic material. It is always preferable to use filtered solutions for processing.

Combined artefacts in the histologic section and photographic emulsion occur if parts of the former are retained on the emulsion surface after separation. Development, especially, is then impaired. The same risks are present in mounted and nuclear emulsion autoradiographs.

In correct autoradiographic work it is necessary to pay due regard to careful 'photographic hygiene'. For example, dust from dried drops of developer and fixer may adhere to the film surface and disturb the processing. Scrupulous cleanliness in the dark room is good practice.

Prevention and Interpretation of Artefacts

In the introduction it was pointed out that about one half of the autoradiographs in the author's work had minor or major artefacts. The great significance of artefacts is therefore evident, and their high incidence is mainly due to the fact that there are so many occasions on which they may affect the work. The greatest care must be taken therefore, in autoradiographic practice, not only if quantitative autoradiography be employed, but also for qualitative conclusions.

Because it is often very difficult to interpret the existence of certain artefacts, an autoradiographic conclusion must not be regarded as final until it has been confirmed on several pieces of film, and preferably, in several animals or specimens.

The most important preventive measures may be summarized thus:

(1) Clean radioisotope solutions must be used for injection.

(2) Great care must be taken in the choice of the histologic fixing agents.

(3) Careful histologic mounting must be employed.

(4) The emulsion surface should not be touched with the fingers.

(5) Only moderate pressure must be applied during the exposure.

(6) Mechanical injury to the film during the wet processing is to be avoided.

(7) Fresh and clean filtered solutions must be employed for development and fixation.

(8) No dust must be allowed to fall on the sections, the film or into the developing and fixing baths.

(9) Controls on sections of tissues without radioisotope should always be made.

(10) Spotless cleanliness in the dark room must be maintained.

SUMMARY

Of the artefacts which occur in autoradiography, a number may be controlled and prevented. These are enumerated and discussed in detail in relation to the various methods of autoradiography employed.

ZUSAMMENFASSUNG

Gewisse Artefakte, die bei der Autoradiographie entstehen, können bemeistert und vermieden werden. Diese werden aufgezählt und im Einzelnen bei verschiedenen angewendeten Autoradiographiemethoden besprochen.

RÉSUMÉ

Parmi les artéfacts qui se produisent dans l'autoradiographie, certains peuvent être évités et prévenus. Ils sont énumérés et étudiés en détail en fonction des diverses méthodes d'autoradiographie employées.

REFERENCES

1. Aminoff, U., Magnusson, G. and Odeblad, E.: Iakttagelser på ovarier och vagina hos mus med stripfilm-autoradiografi. (Swedish.) Nord. Med. 48 (1952), 1123.
2. Bélanger, L. F.: A Method for Routine Detection of Radiophosphates and Other Radioactive Compounds in Tissues. The Inverted Autograph. Anat. Rec. 107 (1950), 149.
3. Bélanger, L. F. and Leblond, C. P.: Method for Locating Radioactive Elements in Tissues by Covering Histological Sections with Photographic Emulsion. Endocrinology 39 (1946), 8.
4. Bonner, N. A. and Kahn, M.: Some aspects of the behaviour of carrierfree tracers. 2. Nucleonics 8 (1951), Febr. p. 46 and March p. 40.
5. Boyd, G. A. and Board, F. A.: A Preliminary Report on Histochemography. Science 110 (1949), 586.
6. Boyd, G. A. and Levy, H.: Carbon 14 beta Track Autoradiography. Science 111 (1950), 58.
7. Doniach, I. and Pelc, S. R.: Autoradiograph Technique. Brit. J. Radiol. 23 (1950), 184.
8. Endicott, K. M. and Yagoda, H.: Microscopic Historadiographic Technique for Locating and Quantitating Radioactive Elements in Tissues. Proc. Soc. Exper. Biol. & Med. 64 (1947), 170.
9. Evans, T. C.: Radioautographs in Which the Tissue is Mounted Directly on the Photographic Plate. Proc. Soc. Exper. Biol. & Med. 64 (1947), 313.
10. Fink, R. M.: A New Approach to High Resolution Radioautography. Science 114 (1951), 143.
11. Gomberg, H. J.: A new High-Resolution System for Autoradiography. Nucleonics 9 (1951), Oct. p. 28.
12. Harrison, G. E. and Raymond, W. H. A.: Preparation of Clean Chemical Solutions with Special Reference to Radioactive Phosphorus Solutions for Clinical Use. Brit. M. J. 2 (1951), 930.
13. Herz, R. H.: Photographic Fundamentals of Autoradiography. Nucleonics 9 (1951), Sept. p. 24.
14. Hevesy, G.: Radioactive indicators. Interscience Publ., New York 1948.
15. Holmes, B. E.: The Indirect Effect of X rays on the Synthesis of Nucleic Acid in vivo. Brit. J. Radiol. 22 (1949), 487.
16. James, T. H. and Higgins, G. C.: Fundamentals of photographic Theory. Wiley and Sons, New York 1948.
17. Jorpes, J. E., Odeblad, E. and Boström, H.: An autoradiographic study on the distribution of Se^{75}-labelled sodium selenate in the rat. To be published (1953).

18. Lacassagne, A. and Lattes, J. S.: Méthode auto-histo-radiographique pour la détection dans les organes du polonium injecté. Compt. rend. Acad. d. Sc. 178 (1924), 488.
19. Lamerton, L. F. and Harriss, E. B.: Some Autoradiographic Studies of Non-uniform Distribution of Radioactive Phosphorus in Tissues. Brit. med. J. 2 (1951), 932.
20. Leblond, C. P.: Metabolism of C^{14}-labelled Steroids. Ciba Foundation Conference of Isotopes in Biochemistry. J. & A. Churchill Ltd, London 1951.
21. Leblond, C. P., Percival, W. L. and Gross, J.: Autographic Localisation of Radioiodine in Stained Sections of Thyroid Gland by Coating with Photographic Emulsion. Proc. Soc. Exper. Biol. & Med. 67 (1948), 74.
22. Leblond, C. P., Wilkinson, G. W., Bélanger, L. F. and Robichon, J.: Radioautographic Visualization of Bone Formation in the Rat. Am. J. Anat. 86 (1950), 289.
23. Marton, L. and Abelson, P. H.: Tracer micrography. Science 106 (1947), 69.
24. Mees, C. E. K.: The Theory of the Photographic Process. Mc Millan Co., New York, 1948.
25. Odeblad, E.: Contributions to the Theory and Technique of Quantitative Autoradiography with P^{32} with Special Reference to the Graafian Follicles in the Rabbit. Acta radiol. Suppl. 93 (1952).
26. — A study of the Short-time Effects on the Mouse Ovary of Internal Irradiation with P^{32}. Acta radiol. 38 (1952), 33.
27. — Unpublished work (1952).
28. Palm, E.: On the Phosphate Exchange between the Blood and the Eye. Acta ophth., Suppl. 32 (1948).
29. Pelc, S. R.: Autoradiograph Technique. Nature 160 (1947), 749.
30. — Radiation dose in Tracer Experiments involving Autoradiography. Ciba Foundation Conference on Isotopes in Biochemistry. J. & A. Churchill Ltd, London 1951.
31. Winteringham, F. P. W., Harrison, A. and Hammond, J. H.: Autoradiography with Water-soluble Tracers in Histological Sections. Nature 165 (1950), 149.
32. Yagoda, H.: Radioactive Measurements with Nuclear Emulsions. Wiley and Sons, New York 1949.

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TECHNIQUE OF ABDOMINAL AORTOGRAPHY

by

Erik Lindgren

Lumbar aortography may be performed by various methods. The procedure generally employed seems to be that originally described by Dos Santos. The patient lies in the prone position and the aorta is punctured directly from the dorsal aspect. If the entire abdominal aorta and its branches are to be investigated, the puncture should be made immediately under the twelfth rib, approximately four fingers-breadth to the left of the midline. The needle is inserted obliquely upwards and inwards with the shaft tangentially to the vertebral column. For the purposes of orientation the point of the needle may be so directed that it first touches a vertebra, and then shifted ventrally until it slides past the body of the vertebra. When the needle is subsequently advanced the aorta is encountered, as a rule, without difficulty. If the site of the puncture has been selected too far medially, or the aorta lies farther to the right than usual, the needle may pass, however, to the left of the vessel. On the other hand, if the puncture site is too lateral, it is possible that the needle, when advanced ventrally towards the body of the vertebra, may in certain cases pass between it and the aorta. If for some reason it is necessary that the puncture site be made extra high, it may lie in the interspace between the eleventh and twelfth ribs. In such a case it is advisable to take a preliminary roentgenogram in order to obtain some idea of the position of the pleura in relation to the ribs. In certain cases the needle probably passes through the most inferior part of the pleural cavity; if patients, the day following a high puncture of the aorta, are examined, a small quantity of fluid may sometimes be observed in the pleura. The amount present is generally so small that it can only be observed in a roentgenogram taken with the patient in the left lateral position; it does not appear to cause clinical

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symptoms. In isolated instances, when a large tumour on the left side of the abdomen might have been punctured by the needle before it reached the aorta, I have attempted to substitute an approach of the aorta from the right side. Perhaps this appears impossible a priori, inasmuch as the needle, when introduced from the right, should first encounter the vena cava. However, in four cases the aorta was entered in the same manner as when the puncture was made from the left, although in a fifth case, the aorta was not encountered.

When the aorta is punctured and the tip of the needle lies freely in the vessel, arterial blood spurts from the mount. Because of the oblique direction of the puncture, however, the tip may lie just at the arterial wall. In certain instances the mouth of the bevel of the needle may even lie partially in the wall and partially in the lumen. The longer the bevel, the more easily will this occur. Arterial blood will be obtained even under these conditions, however, although the flow will be somewhat less. The rate of flow of blood from the needle is essentially dependent upon the blood pressure, and it may be difficult therefore, to determine the position of the extremity of the needle from the rate of flow alone. If the needle bevel lies partially in the vessel wall, some of the contrast medium naturally will enter the aortic wall on injection. Even if a trial injection of a small quantity of contrast medium shows it all to enter the lumen of the vessel, some of the contrast substance may nevertheless be injected paravascularly during the main injection. This accident may depend upon several factors. If the injection is made with great force, a purely mechanical displacement of the needle in relation to the aortic wall may occur. Nor can the possibility be dismissed that a rapid injection of a very hypertonic solution may cause contraction of the vessel, with the result that the needle tip, if situated close to the wall, may be displaced into its substance.

On repeated occasions, judging from the literature, a vessel other than the aorta has been punctured. WAGNER & PRICE have reported a case in which the contrast medium was injected into the superior mesenteric artery, with a resulting fatal mesenteric thrombosis. A renal artery has also been punctured instead of the aorta, and the contrast medium injected directly into it rather than into the latter. Parenchymal necrosis in the kidney following such injections has been described (DOS SANTOS; DUCUIN, PONS & ENJALBERT). The unfortunate sequelae of these injections have certainly been caused by the use of unsuitable contrast media. However, even if no serious consequences had occurred, the examinations would certainly have been unsuccessful and failed to provide the information desired. It is clearly evident from the reports in the literature and from own experience that the procedure normally employed in aortic puncture is accompanied by certain disadvantages.

Dos SANTOS mentions a 'zone dangereux', in which the puncture must not be performed. This zone is supposed to correspond to the site of the renal arteries. However, it is impossible to be quite sure beforehand where the renal arteries lie, or how many there are. There are even some who prefer to carry out the puncture in just this very region in order that the contrast medium may be injected as close as possible to the renal arteries and that filling of the hepatic and lienal arteries may be avoided (WICKBOM). If this procedure is used, however, a test injection must always be made to determine the exact position of the needle before the main injection is undertaken. If lumbar aortography is to be performed by direct percutaneous puncture, the most satisfactory procedure seems to be the following: When the aorta has been entered and blood flows out from the mount of the needle, a slender metal stylet is introduced into the bore. This stylet is provided with a movable stop-screw, adjusted so that when the former is inserted as far as the latter will permit, the tip of the stylet lies in the mouth of the bevel. The stop-screw is then moved back a few millimeters and the stylet advanced. In this manner, the distance from the tip of the needle to the opposite aortic wall is determined. It should be from 4 to 5 mm. When this condition is attained, the position of the puncture needle is fixed in relation to the skin with another stop-screw to prevent displacement of the needle during the injection. If it is possible to advance the stylet 1 cm or more, it means that the extremity has slipped into a vessel arising from the aorta or that a vessel other than the aorta has been punctured. Accordingly, such a needle position is unisatisfactory and the puncture should be repeated. On the other hand, if the stylet cannot be advanced at all or only about a millimeter, it is an indication that the needle tip lies so near the aortic wall that injection of the contrast medium is inexpedient. It is thus possible, with the aid of the stylet, to arrive at a satisfactory position of the needle tip in the lumen of the aorta. Its position in relation to the branches of the aorta, however, is determined only after a test injection of a small quantity of contrast substance, *e. g.*, 8 to 10 cc of a 50 per cent water-soluble contrast medium. In the roentgenogram taken during this injection it is possible to observe the position of the needle tip in relation to those vessels which it is especially important to visualize in the particular case. If necessary, the needle position may be corrected after this preliminary roentgenogram is viewed. In my experience this procedure is the only one which guarantees that the point of the needle lies in such a position in the aorta that injection of contrast medium paravascularly or into the aortic wall will be avoided and the injection made at the correct site in the aorta. The performance of a test injection alone is not always satisfactory. If the tip of the needle does not lie correctly in the lumen of the vessel, some of the contrast

medium may be injected into the wall. On the other hand, notwithstanding a successful test injection, the main injection, for the reason stated, may be partially extra-aortic. During the development of the preliminary film and the preparations for the main injection, physiologic saline solution is injected. In cases in which only the division of the aorta and the vessels distal to it are to be investigated, the puncture should be made approximately at the level of the third or fourth lumbar vertebrae *i. e.*, lower than described earlier; this is in order that the contrast medium shall be concentrated in the arteries to be examined rather than pass into the large abdominal vessels.

Direct puncture of the aorta involves certain hazards. This fact induced FARIÑAS to perform what he called retrograde abdominal aortography. He exposed the femoral artery, inserted a catheter up into the aorta, and injected the contrast medium through the catheter. EULER has described another method. This seems unnecessarily involved however, and does not appear to offer any advantages. It consists in puncturing the aorta through the oesophageal wall via an oesophagoscope. Finally, a catheter, introduced after exposure of the radial artery, may be passed up into the aorta, down through the thoracic aorta and into the abdominal aorta. In the latter procedure it is usually necessary to ligate the radial artery. Even if suture of the vessel is carried out, the artery does not appear to be permeable to the blood stream distal to the site at which the catheter is introduced. If FARIÑAS' method is used, the artery must be sutured after the catheter is withdrawn. The surgical procedure then becomes relatively extensive. It is possible, however, to introduce a surprisingly thick trocar percutaneously into the femoral artery without notable coincident haematoma formation or postinjection haemorrhage. A polyethylene catheter may then be introduced via this trocar. Catheters of this material have a relatively large internal in relation to the external diameter. Consequently catheters permitting a sufficiently rapid injection of a large quantity of contrast medium may be employed. The catheters used earlier had the advantage of roentgen opacity, it is true, but the walls were so thick that it was impossible to introduce a catheter of adequate bore in this manner. After the procedure is completed, a compression dressing is applied. On the other hand, if the artery is exposed, the vessel walls do not contrast and the hole left by the trocar remains open, necessitating suture of the vessel. To facilitate the introduction of the trocar, it may be expedient in many cases to make a small incision through which the operator can insert one finger against the vessel, thus determining its position. The trocar is then inserted percutaneously, about 2 cm distal to the incision, down to the vessel into which it is to be introduced with the guidance of the finger inserted through the incision. When the needle is in a satisfactory position, the

incision is sewn up. At the termination of the investigation the trocar may be removed in the same manner as if no incision had been made. Suture of the vessel is thus unnecessary and the operation of such a scope that it may be performed by the roentgenologist himself. To facilitate entrance into the artery, the trocar should be slightly curved and in addition, a rubber tube a few centimeters in length should be attached to the end. As soon as the blood starts to flow out through the trocar, this tube should be compressed by the fingers until the catheter is introduced. If the width of the catheter is correct in relation to the diameter of the trocar and rubber tube, no blood will leak out around it nor creep outside the trocar. On the other hand, if the trocar is withdrawn after the catheter has been inserted, blood will usually seep out along the catheter; the trocar should be left therefore, in position during the examination. If a straight trocar is used, it may be difficult to enter the vessel and further, the catheter must kink relatively sharply at the extremity of the trocar in order to pass up in the vessel. As a result of this the catheter usually becomes caught in the vessel wall. One disadvantage of these catheters is the lack of roentgen opacity, thus precluding any direct observation of their position. However, either by inserting a fine metal wire along the bore or by injecting a small quantity of contrast medium, the position of the tip of the catheter may be determined. This procedure also affords information concerning its position in relation to the branches of the aorta. The catheter method may seem somewhat more circumstantial, but on the other hand, it guarantees that no extra-vascular escape of contrast medium takes place and permits easy determination of the exact site of injection in relation to the vessels arising from the aorta. Another advantage with the catheter method is that the patient lies in the supine position. If urography has demonstrated a hydronephrosis, the patient should be examined aortographically in order to determine whether or not the hydronephrosis is caused by an aberrant vessel. After the aortographic films have been taken, no movement of the patient is permitted. The injected contrast medium is gradually excreted into the renal pelvis and, as the patient's posture is unaltered, visualization of the exact relationship of the renal pelvis to the renal vessels is possible. In the supine position the filling of the anterior branches of the aorta is not so dense, due to the weight of the contrast medium, as when the patient lies in the prone position. This is a great advantage inasmuch as branches of the superior mesenteric artery are frequently projected over the kidneys. The insertion of the catheter through the femoral artery up into the aorta has also the advantage over its insertion through the radial artery in that the contrast medium in the former case will be injected against the blood stream. The contrast will then be more concentrated

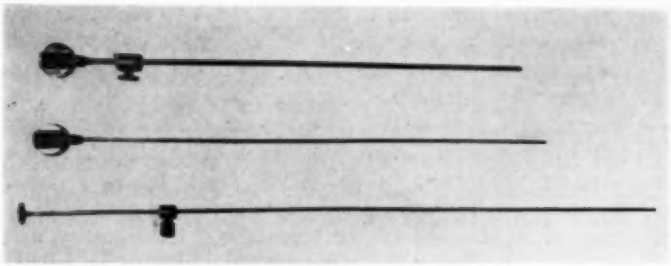


Fig. 1. Instrumentarium for direct — percutaneous — aortography
Above: Puncture needle with movable stop-screw.
Middle: Mandrin, which remains in the needle until it approaches the aorta.
Below: Stylet with movable stop-screw for determination of the position of the needle tip.

than when injected in the same direction as the blood flow. The rate of injection must, in this latter case, be much more rapid if the same concentration of the contrast medium is to be obtained. An additional advantage is that general anaesthesia is easier to administer with the patient supine. In the case of stenosal vascular changes in the distal part of the aorta or in the iliac arteries, however, retrograde catheter insertion cannot be employed.

In general, the interest of those engaged in aortography appears to centre essentially upon the appearance and situation of the arteries, for which a particularly large diameter of puncture needle or catheter is unnecessary. In the examination of the kidneys, however, visualiza-

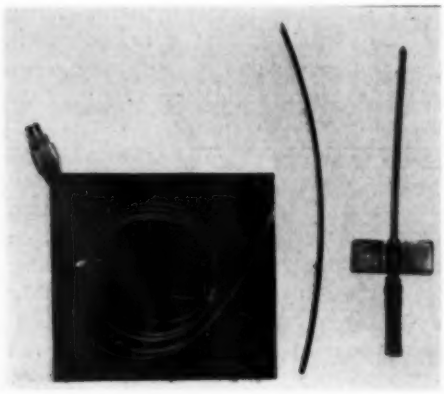


Fig. 2. Instrumentarium for the catheter method.
Middle: Mandrin: also showing curvature of the trocar.
Right: Trocar with rubber tube.
Left: Polyethylene catheter with coupling device.

tion of the arteries is only one part of the investigation, and the least essential. The more important matter is the study of the filling of the kidneys — the nephrographic effect. The increased density in the renal parenchyma, called the nephrographic effect, occurs when the contrast medium has left the arteries and lies partially in the capillaries and partially in the renal parenchyma, in the course of being excreted. For an optimal nephrographic effect, a relatively rapid injection rate must be possible, otherwise the contrast medium will be excessively diluted by the blood in the aorta. If direct puncture is used, the internal diameter of the needle should be 1.2 mm. The contrast medium may be injected manually through such a needle, but some device to facilitate the injection and regulate the rate is preferable. If the catheter method is used, the resistance is greater and, in my experience, a satisfactory rate of injection is not obtained by hand; the injection must be performed therefore with a special injection apparatus. Dos SANTOS has described a device by which the contrast medium is forced in by means of compressed air. DOSS mentions a similar method. In my opinion, there are certain inherent disadvantages: Satisfactory pressure is not maintained and is not constant during the injection because of the small volume of the compressed air. Moreover, the latter is in direct contact with the surface of the contrast medium. If the operator is negligent, or if the shut-off valve breaks down, it is conceivable that compressed air may be forced into the arterial system. To eliminate the risk of this occurring, CHRISTOPHE has suggested an apparatus in which the plunger of the syringe is pressed down by a rod cogged at one end and geared to an electric motor. The roentgen exposure takes place automatically, by means of a contact mounted on the rod. I prefer and employ an apparatus which may be described as a combination of the two. It is shown in Figs. 3 and 4. A 50 cc syringe is mounted in a plastic holder. Compressed air operates the plunger of the syringe and is thus not in contact with the surface of the fluid. The volume of air is so great that a constant pressure is maintained during the injection. A contactor controls the exposure, permitting its release after an optional quantity of contrast medium has been injected. The device is placed in a special holder on the examination couch. When the catheter has been inserted it is attached to the injection syringe, the operator subsequently withdrawing from the field of the roentgen ray exposure. (The apparatus is made by Elema-Järnh Ltd.)

Some writers still use sodium iodide in 80 to 100 per cent solutions as a contrast medium. However, it is highly irritative and is certainly the source of the complications described when a contrast substance is injected into vessels other than the aorta. The 70 per cent water-soluble contrast media of the Umbradil, diodrast and diodone type employed to-day, are considerably better and do not appear to produce ill-effects

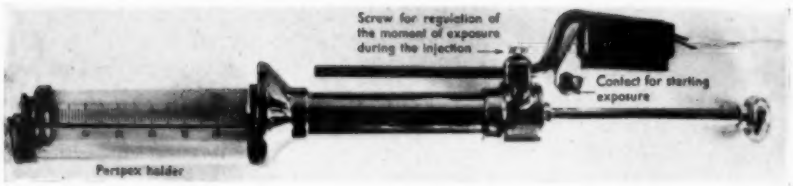


Fig. 3. Injection apparatus; 50 cc syringe.

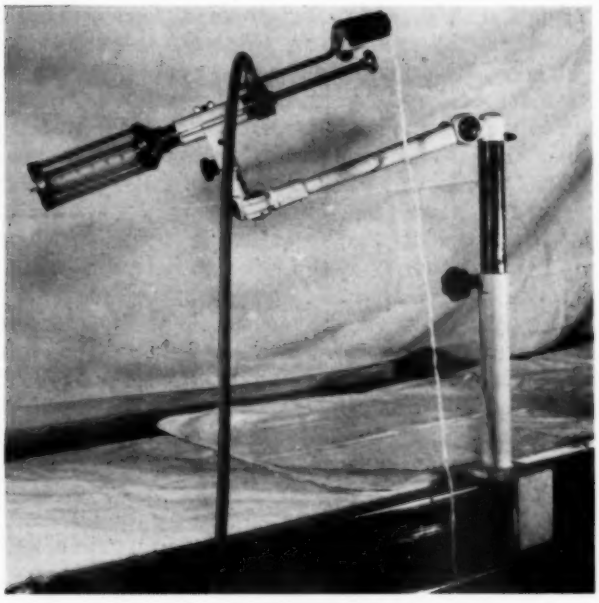


Fig. 4. Apparatus mounted on the examination couch.

even if injected into vessels other than the aorta. In patients who are not too heavy, even a 50 per cent solution of the contrast agent results in satisfactory films if the technique is good. The quantity employed should be approximately 40 cc injected within a maximum period of 6 to 7 seconds. When the contrast medium is introduced via a catheter inserted in a retrograde direction and the injection time is very short, a kind of embolus of contrast substance at first forms at the tip of the catheter. An instant later, however, this is dispersed in the aorta by the blood stream. If the injection time is about 5 seconds or more,

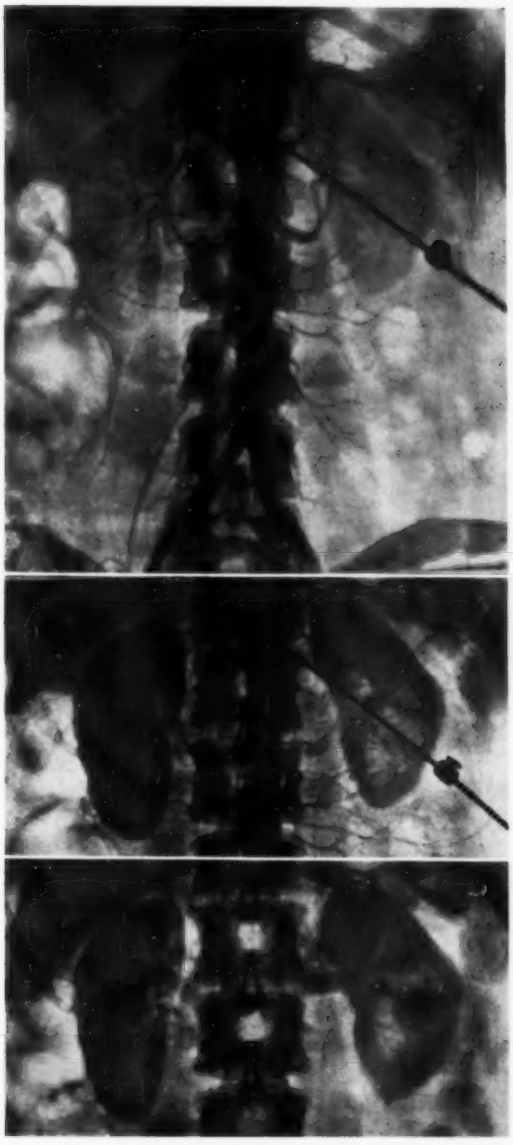
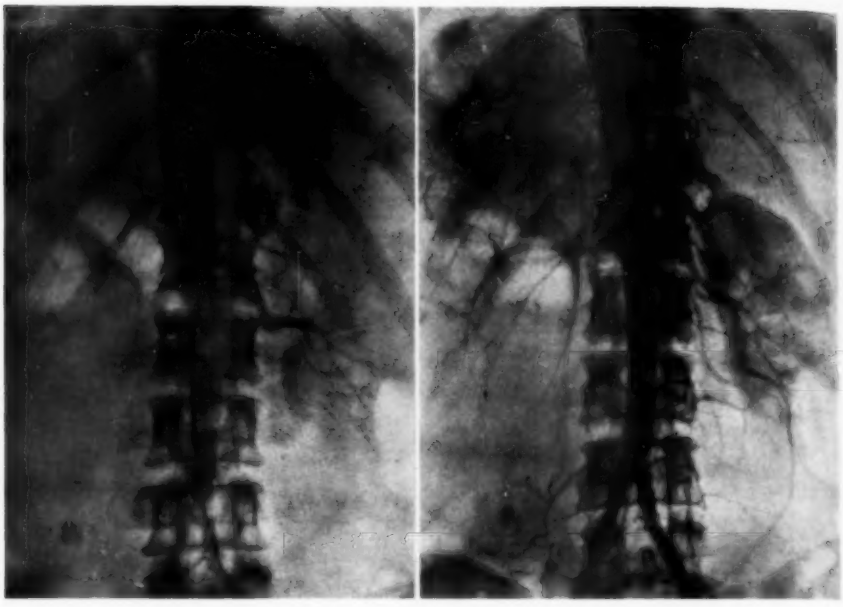


Fig. 5. Normal aortography — percutaneous method
a) Arterial phase: b) nephrography, early stage,
c) venous phase; nephrography, late stage.



a. b.

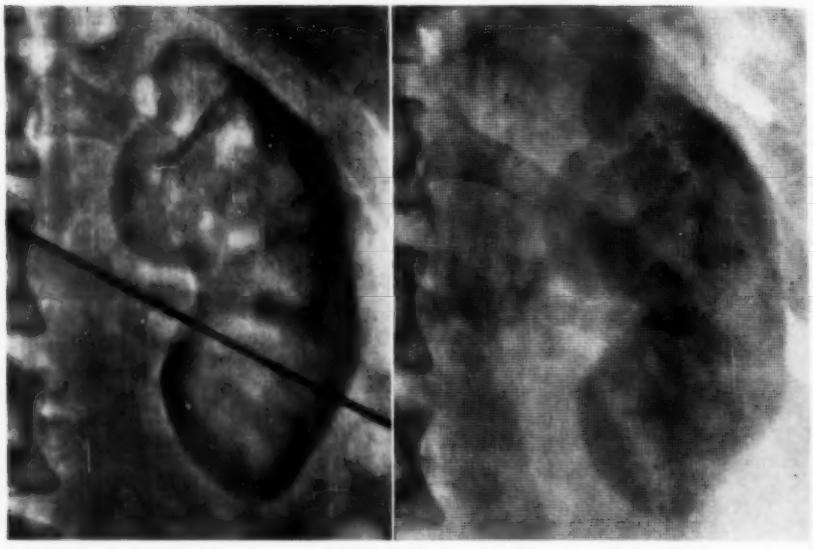
Fig. 6. Aortography — catheter method. Injection pressure: 8 atmospheres. Blood pressure: 85 mm Hg systolic. Catheter 240. a) The contrast medium lies like a pillar at the tip of the catheter. The exposure was made after 20 cc of contrast medium had been injected. b) The contrast medium has been dispersed by the blood flow in the aorta and its branches, 1 second later.

such an embolus does not occur. The nephrographic effect will not be as clear and the possibility of visualizing the renal veins will be less if the injection time is relatively long. It is this need for the rapid introduction of a large quantity of contrast medium which necessitates puncture needles and catheters of sufficiently large internal diameter. Polyethylene catheters of size number 240 or 200 may be used in the examination of adults. With the injection apparatus described and a number 200 polyethylene catheter, a pressure of 7 to 8 atmospheres is necessary to produce the aforementioned rate of injection when the systolic blood pressure is approximately 85 mm Hg.

The investigation may be performed under either local or general anaesthesia. Local anaesthesia may be used with direct injection or catheter insertion. However, if there are no contraindications, I prefer general anaesthesia as readily permitting a suitable level of blood pres-

Fig. 7. Aortography — catheter method. Injection pressure: 6½ atmospheres. a) Exposure was made after 20 cc of contrast medium had been injected (cf. fig. 6 a).

sure during the period of injection of the contrast medium to be obtained. That is to say, the nephrographic effect will be greater if the blood pressure is low. Immediately before the injection of the contrast medium, the anaesthetist lowers the blood pressure to approximately 85 mm systolic pressure. We have obtained the best nephrographic effect at this blood pressure level and with the injection times given. If the pressure is lowered still further, the nephrographic effect will naturally become somewhat more marked. At approximately 70 mm systolic pressure, however, excretion through the kidneys ceases, and it seems inadvisable to lower the blood pressure to a level too near this limit. It is generally stated in the literature that the renal veins cannot be visualized aortographically. However, if the examination is carried out according to the procedure described, the renal veins are usually well filled with contrast medium, and may be observed in films taken 15 to 20 seconds after the injection. The roentgenograms should be obtained with high kilo-voltage — at least 90 to 100 kV — and with as short an exposure time as possible. A good secondary diaphragm is particularly important. The first film is exposed when approximately 20 cc of the



a. b.

Fig. 8. Nephrography. a) Without test injection. b) With test injection. The same patient was examined on the two different occasions; each time the blood pressure was 90 mm systolic. (Tuberculous changes in the upper pole.)

contrast medium have been injected and the injection is being continued. The aorta and its branches are seen outlined in this film. A rapid change of casettes during the next two seconds is valuable. Thereafter, no rapid alteration in the nephrographic appearances occurs, and exposures may be made at intervals of several seconds. The veins are usually not filled with contrast medium until after approximately 15 seconds. If no test injection has been made, the kidney structure is clearly visualized in the nephrographic films. The kidney has the same appearance as in an anatomic preparation, *i. e.*, the cortical layer is clearly delimited from the medullary substance. If a test injection has been performed, however, the kidney will present a more homogeneous appearance after the main injection (see Fig. 8). This is because the contrast medium injected in the test injection has been partially excreted by the time the main injection is made, and lies in the renal canals. This contrast medium, together with that injected later, which lies in the capillaries and parenchyma, produces a largely homogeneous appearance of the kidney.

It is reported in the literature that contrast substances have been injected paravascularly around the aorta, on many occasions, without

apparently having caused complications other than pain of a relatively transient nature. HENLINE and MOORE, however, have observed separation of the layers of the aorta and death from traumatic haemorrhage in dogs. To the best of my knowledge, such observations are unknown in the clinical use of aortography, but the investigations aforementioned emphasize that the injection of contrast medium into the aortic wall should be avoided. And, if the examination is performed according to the principles outlined, it can be avoided. With the catheter method all risk of injection into the vessel wall or paravascularly, of course, is eliminated. Aortography is contraindicated essentially only by hypersensitivity to the contrast medium or by impaired renal function. Accordingly, the patient should have been tested for possible hypersensitivity before the examination. This should be done by the injection of 2 cc of the contrast substance intravenously the day before the aortographic examination; this is by reason of the fact that, in our experience, reactions may occur several hours after the injection. In one case no reaction was observed until five hours had elapsed. We have found that neither cutaneous tests nor the instillation of small quantities of the contrast agent into the conjunctival sac are, in this instance, of value as tests for hypersensitivity.

Successful lumbar aortography depends on the appreciation of the principles involved as well as meticulous care in the essential details of technique. Provided that these conditions are observed, the investigation may be said to be safe to employ freely as an advanced diagnostic procedure.

SUMMARY

The various techniques of abdominal aortography are discussed. A modification of the catheter method and a new apparatus for injection are described.

ZUSAMMENFASSUNG

Die verschiedenen Methoden der abdominalen Angiographie werden diskutiert. Eine Modifikation der Kathetermethode und eine neue Injektionsapparatur wird beschrieben.

RÉSUMÉ

L'auteur étudie les différentes techniques d'aortographie abdominale. Il décrit une modification de la méthode par cathétérisme, ainsi qu'un nouvel appareil d'injection.

REFERENCES

CHRISTOPHE, L. & HONORÉ, D.: L'artériographie par injection et prises de clichés automatiques. J. de chir. 63 (1947), 5.

DENSTAD, T.: Abdominal aortography. Acta radiol. 38 (1952), 187.

Doss, A. K.: Translumbar aortography; its diagnostic value in urology. J. Urol. 55 (1946), 594.
Dos Santos, R.: L'aortographie dans les tumeurs rénales et pararénales. Arch. mal. des reins 8 (1934), 313.
Ducuing, J., Pons, H. & Enjalbert, A.: L'aortographie abdominale. J. de radiol. et d'électrol. 30 (1949), 497.
Euler, H. E.: Die peroesophagale Aortenpunktion, ihre diagnostischen und terapeutischen Möglichkeiten. Arch. f. Ohren-, Nasen- u. Kehlkopfk. 155 (1949), 536.
Fariñas, P. L.: Retrograde abdominal aortography. Radiology 47 (1946), 344.
Henline, R. B. & Moore, S. W.: Renal aortography, preliminary report of experimental study. Am. J. Surg. New series 32 (1963), 222.
Larsson, H. & Palmlöv, A.: Abdominal aortography with special reference to its complications. Acta radiol. 38 (1952), 111.
Leroux, G. F.: Intérêt de l'aortographie et de l'artériographie femorale etc. J. de radiol. et d'électrol. 29 (1948), 251.
Melick, W. F. & Vitt, A. E.: The present status of aortography. J. Urol. 60 (1948), 321.
Peirce, E. C.: Percutaneous femoral artery catheterization in man with special reference to aortography. Surg., Gynec. & Obst. 93 (1941), 56.
Runström, G.: Aortografi. (Swedish.) Nord. med. 38 (1948), 934.
Sante, L. R.: Evaluation of aortography in abdominal diagnosis. Radiology 56 (1951), 183.
Wagner, F. B.: Arteriography in renal diagnosis etc. J. Urol. 56 (1946), 625.
Wagner, F. B., Price, A. H. & Swenson, P. C.: Abdominal arteriography. Technique and diagnostic application. Am. J. Roentgenol. 58 (1947), 591.
Wagner, F. B. & Price, A.H.: Fatality after abdominal arteriography. Surgery 27 (1950), 621.
Weyde, R.: Abdominal aortography in renal diseases. Brit. J. Radiol. 25 (1952), 353.

FROM THE II MEDICAL CLINIC (DIRECTOR: PROF. E. HAYNAL) OF THE UNIVERSITY OF BUDAPEST, HUNGARY

PERMANENT DEPOSITION OF IODINE CONTRAST MEDIUM IN THE WALL OF THE STOMACH

by

Albert Bogsch

During the course of a roentgen examination of a patient suffering from obstructive jaundice, certain unusual signs were encountered and appear to be worth recording.

L. A., a male patient, aged 62, had suffered, 13 years previously, from recurrent attacks of cholelithiasis. Repeated cholecystographic examinations revealed gall-stones. For eight years the patient remained free from symptoms when, in 1946, due to the obstruction of the common duct, he developed jaundice. Removal of the stones from the common duct and cholecystectomy were performed in December 1946 (RÉKAY).

The year following the operation the patient was well and regained his former weight. However, after a certain period the jaundice recurred and was accompanied by fever. At the site of the operation, a fistula had developed in the abdominal wall and from which bile escaped. The formation of this fistula brought a few months' improvement but upon its closure the jaundice became more marked.

The patient came to our clinic in July, 1949 in this condition. During the course of treatment, duodenal drainage had been attempted and the failure of the latter necessitated a roentgen examination in order to ascertain whether the tube was in correct position in the duodenum.

The roentgen examination revealed a most unusual picture. Around the tube, without any previous administration of contrast medium, the lower two-thirds of the stomach and its mucosal pattern were excellently outlined (Fig. 1). This portion of the stomach was more opaque than the vertebral column; it was granular in structure and

Fig. 1. Routine roentgenogram of stomach before the administration of barium.

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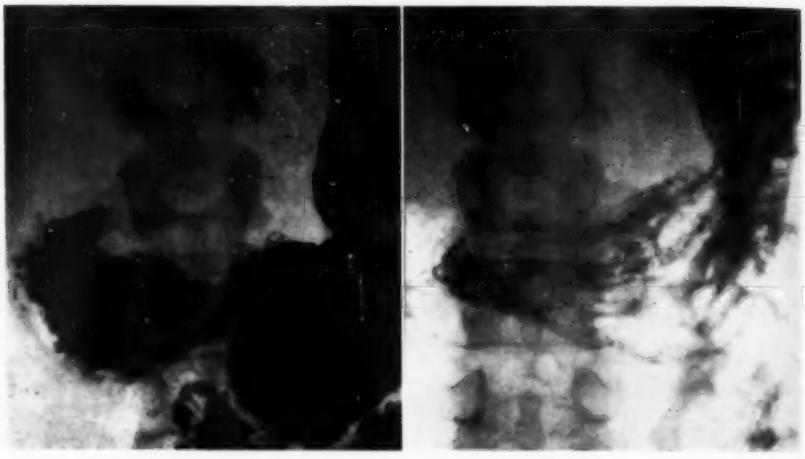


Fig. 2. Barium meal. Note opaque substance in the stomach wall.

exhibited normal peristaltic movements. To the right of the stomach in about the site of the gall-bladder and bile ducts, three shadows were discernible, each about the size of a grain of rice. A later operation proved these to be gall-stones in the common bile duct. I repeated these plain radiographic studies of the stomach three times with a few days' interval between each and the result was always the same.

The patient's statement that as far as he was aware he had not been given any contrast-producing drug immediately before the roentgen examination, and the re-examination of the stomach following the administration of barium, only tended to confirm that the shadow in the plain radiogram was situated in the wall of the stomach. Besides the dense homogeneous shadow of the barium-filled stomach, the roentgen examination (Fig. 2) revealed a contrast band running parallel with the outline of the stomach and separated by a narrow shadow of soft tissue from its lumen. Deep peristaltic waves proved the motility of the stomach. On examination of the mucosa with the aid of diluted barium, the granular structure of the dense stomach shadow was clearly visible in addition to the homogeneous shadow produced by the contrast medium which filled the folds of the mucosa.

Due to the increasing jaundice the patient was subjected to a second operation in October 1949 (BÉLA MOLNÁR).

Extract from the operation record: firm adhesions to the stomach and duodenum noted subhepatically. The common duct was distended to about the width of a thumb and on puncture, turbid purulent bile exuded. After choledochotomy three stones were removed and as the Vater-papilla was obstructed, choledocho-duodenostomy was performed.

During the operation a further investigation of the condition of the stomach was possible. On thorough and careful palpation of the stomach, the walls appeared to be quite soft. This observation contradicted the assumption that the dense stomach shadow could be caused by granular calcification.

On the tenth day following the operation, the patient died. The autopsy (the pathologic examination was performed by ANNA VECSEI) revealed about 1 liter fibrinopurulent fluid in the peritoneal cavity. A gauze strip led to the site of the gall-bladder bed. The common bile duct was distended to about the width of a finger. The cystic duct did not open into the common bile duct in the usual situation, but ran parallel with it nearly as far as the duodenum, the two very distended ducts uniting just before reaching the latter. There was an anastomosis about 1 cm in diameter between the duodenum and the common bile duct. Many adhesions were present in the area of the operation and a considerable amount of the fibrinopurulent fluid lay in this region.

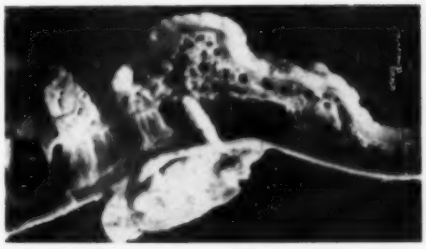


Fig. 3. Section of stomach wall. Spongy structure of the submucosal layer.

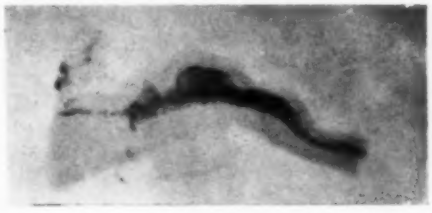
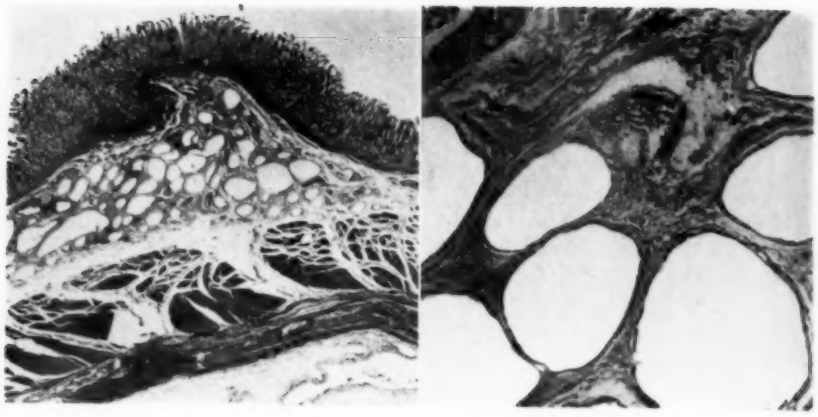


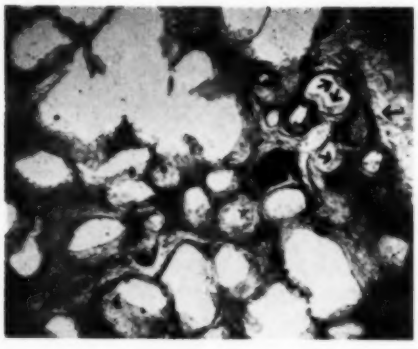
Fig. 4. Roentgenogram of fig. 3 section. The opaque substance also lies in the submucosa.

In the roentgenogram of the stomach preparation the contrast producing grains appear to be more dense, are more clearly defined and can be better distinguished from each other. In certain areas they present, due to projection, a confluent appearance and are situated mainly in the region of the pyloric antrum. On opening the stomach no ulcer or tumour is visible. The fundus is normal.

The wall of the stomach in the region of the antrum and pylorus in the area corresponding to the site of the abnormal opacity, is markedly thickened. The thickening is irregular and has no definite borders. In the cross section preparation the muscle tissue appears to be of normal thickness; no abnormalities are visible in the mucosa but the submucosa layer is increased to 2—4—6 mm in thickness. On inspection this submucosa layer appears to be of a spongy structure and in its substance are rounded cavities of varying size visible to the naked eye (Fig. 3). For the purpose of histologic examination, sections were obtained from different parts of the mucosa. In that region where on naked eye examination the stomach wall was found to be of normal thickness, *i. e.* round the fundus, the micrographic appearances were also normal. The area, however, in which thickening of the submucosa was found, presented an entirely different picture (Fig. 5 a). The mucosa appears to be quite normal even in this situation, the muscular mucosa being of normal thickness but the loose connective tissue of the submucosa contains enormously distended cyst-like structures. Their thin walls are lined with endothelium and the region has the usual number of arteries and veins of normal size. The cavities are most probably dilated lymph vessels. In certain situations they are so distended that they have ruptured into one another. The usual staining methods reveal no clue as to the contents; the cysts appear to be empty. Around the excessively distended lymph ducts, a normal quantity of loose connective tissue of the submucosa is visible but the cells and the interstitial spaces show no abnormality. The marked thickening of the submucosa must, therefore, have been caused exclusively by the enormous distension of the lymph ducts (Fig. 5 b).



a. b.



c.

Fig. 5. Histologic examination.

a. Cyst-like structures in the mucosa.
b. Magnification of *a*.
c. Frozen section stained with Sudan III. The opaque substance is situated in a fatty material in the cavities.

The autopsy and histologic studies thus confirm the surgical findings since neither in the sections nor by Kossa's staining could any trace of calcification be demonstrated.

From the above observations the question arises as to the nature of the abnormal gastric opacity; it could not have been caused by the cystic structures. The cavities of the spongeous layer and the grains of the densities are identical in size and shape and both lie in the submucosa (Figs. 3—4). We may infer from these data that the contrast producing substance must be sought, after all, in the cavities of the submucosa. A frozen section, stained with Sudan III revealed that there

was a fatty substance in the cavities, which during embedding was washed out from the preparation (Fig. 5 c).

Having exhausted the histologic procedures we had to turn to chemistry. The Municipal Institute of Chemistry (Dr. AJTAY) demonstrated the presence of 42 mg iodine in a stomach particle of 1.75 g. Apart from the cholecystographic examinations (1946), there had been no data in the patient's history suggesting the administration of any drug containing iodine in any quantity. It may be assumed, therefore, that the iodine penetrated the wall of the stomach, *i. e.* into the dilated lymph ducts during the cholecystographic examinations and remained deposited there for three years. Unfortunately at the time of our examination it was impossible to determine whether the cholecystographic examinations were performed intravenously or perorally; the type of drug administered could also not be ascertained.

No definite answer can be given to the question as to the manner in which the iodine contrast medium penetrated into the submucosa of the stomach particularly in the antral region. According to the pathologist, the cause may be explained by anatomic considerations. Cicatrized adhesions, found subhepatically, were doubtlessly the result of repeated inflammation around the gall-bladder. The cystic and common bile ducts were markedly distended by stones, and were embedded tightly in the surrounding connective tissue. Lymph ducts had grown into this tissue, which owing to the position of the adhesions ran to the nearest part of the stomach, *i. e.* to the region of the antrum and pylorus. When contrast medium was introduced into the gall-bladder and ducts, and the presence of stones prevented its evacuation, it filled the lymph vessels leading to the stomach wall. The thin-walled, easily distensible lymph ducts became occluded as a result of inflammation, and the contrast medium remained deposited for a protracted period to be disclosed three years later on roentgen examination.

SUMMARY

The author describes and discusses the finding of certain opaque substances in the wall of the stomach found during an abdominal radioscopy which were proved to have arisen from an iodine contrast medium deposited on the occasion of cholecystography some three years previously. An explanation of the method of deposition is advanced.

ZUSAMMENFASSUNG

Der Verf. beschreibt und diskutiert die Entdeckung gewisser opaker Substanzen in der Magenwand, die bei einer leeren Bauchdurchleuchtung gemacht wurde. Man stellte fest, dass diese Substanzen von einen Jodkontrastmittel herstammen, welches anlässlich einer Cholezystographie vor 3 Jahren gegeben wurde. Für den Depositionsmodus wird eine Erklärung abgegeben.

RÉSUMÉ

L'auteur décrit et étudie des opacités siégeant dans la paroi de l'estomac, découvertes à l'occasion d'une radioscopie de l'abdomen; il montre qu'elles proviennent du dépôt d'un produit de contraste administré pour une cholécystographie environ trois ans auparavant. Il propose une explication du mécanisme de dépôt.

REFERENCES

1. Abel, W.: Zur Diagnose der Magenwandverkalkungen. Fortschr. Röntgenstr. 59 (1939), 64.
2. Beliczay-Pavlik, M.: Kiterjedt meszesedés a gyomor falában (Hungarian). Magyar Röntgen Közlöny 11 (1937), 145.
3. Henke, F. & Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, IV (1926). Springer, Berlin.
4. Imbert, R.: Linite et calcification gastrique. Bull. Soc. Radiol. méd. France 19 (1931), 351.

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LUMBOSACRAL TRANSITIONAL VERTEBRAE

A Clinical and Roentgenologic Study of 400 Cases of Low Back Pain

by

E. Hasner, H. H. Jacobsen, M. Schalimtzek and *E. Snorrason*

The relationship between low back pain with sciatic radiation and the presence of lumbosacral transitional vertebrae has been the subject of much discussion during the last 20 years, but so far its many pertinent problems have defied definite solution; as REISNER (12) put it, "Many people have transitional vertebrae without low back pain and many have low back pain without transitional vertebrae, but few have both at the same time."

The anatomic conditions have been clarified by TODD (15) and WILLIS (16) in their studies on the mammalian spinal column; in 96 per cent of all human beings, 12 thoracic and 5 lumbar vertebrae are present, making a total of 17 in the thoracicolumbar segment, whereas the modal number of thoracicolumbar vertebrae in lower mammals is 19.

The roentgenographic appearance of transitional vertebrae at the lumbosacral junction of the spine has been studied by GEORGE (3), INGEBRIGTSEN (9), BRAILSFORD (1), FERGUSON (2), MITCHELL (11), and HODGES and PECK (8); GEORGE found that 35 per cent of all spinal columns subjected to roentgen examination showed congenital anomalies.

BRAILSFORD, in a study of the roentgenograms of 3,000 unselected patients, found that 3.4 per cent had unilateral and 4.7 per cent bilateral sacralization. HODGES and PECK examined 447 patients with low back pain: 27 per cent of these had anomalies in the lumbosacral segment as compared with 14 per cent in a symptom-free control group.

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However, the relation of these anomalies to low back pain with sciatic radiation has not been unequivocally clarified. Thus, SIMONS (14) enumerated five different theories without attaching particular preponderance to any of them. In a recent publication, DE SÈZE (13) reported on 206 cases of sacralization and 51 cases of lumbarization; he expressed the view that the pain is referable (1) to dynamically conditioned excessive strain of the intervertebral disk immediately above the abnormal vertebra and (2) to failing balance in the lumbosacral joint due to the generally asymmetric nature of the anomalies. However, he added that transitional vertebrae are present in 6—7 per cent of symptom-free subjects.

In a series consisting of 2,000 patients with backache examined at the Mayo Clinic, GHORMLEY (4) found only two cases in which the pain was due to partial sacralization.

LINDBLOM (10) showed that changes in the tension of degenerated lumbar intervertebral disks give rise to pain of typical distribution in the lumbosacral region and the lower extremities. In view of this observation and the fact that roentgenographic studies of the spinal function may provide information as to anomalies of the intervertebral disks, we investigated the function of the lumbar disks in patients who had both transitional vertebrae and low back pain with sciatic radiation.

Material

A roentgenographic study of 400 patients with a view to investigating the mobility of the lumbar spine (5, 6) revealed sacralization in 30 patients (6 men and 24 women) and lumbarization in 10 patients (1 man and 9 women).

Roentgenograms were taken with the patients in the sitting position with the spine flexed forwards and backwards, respectively as well as on maximal lateral bending (5).

Roentgenographic Appearances. As appears from table 1, changes in the mobility of the lumbar disks was a frequent finding in the presence of sacralization and lumbarization; these changes manifested by parallelism or paradoxical angulation on lateral bending of the spine must be taken as evidence of disturbances of the balance of the lumbar spine. Figs. 1 and 2 illustrate the conditions in a case of bilateral sacralization with left-sided nearthrosis; a paradoxical angulation is seen on bending to the same side as the nearthrosis.

In nine of the ten cases of lumbarization a narrowing of the fifth lumbar intervertebral disk was observed, whereas such a narrowing was encountered only in one half of the cases of sacralization. In some cases lumbarization was accompanied by marginal sclerosis with localized

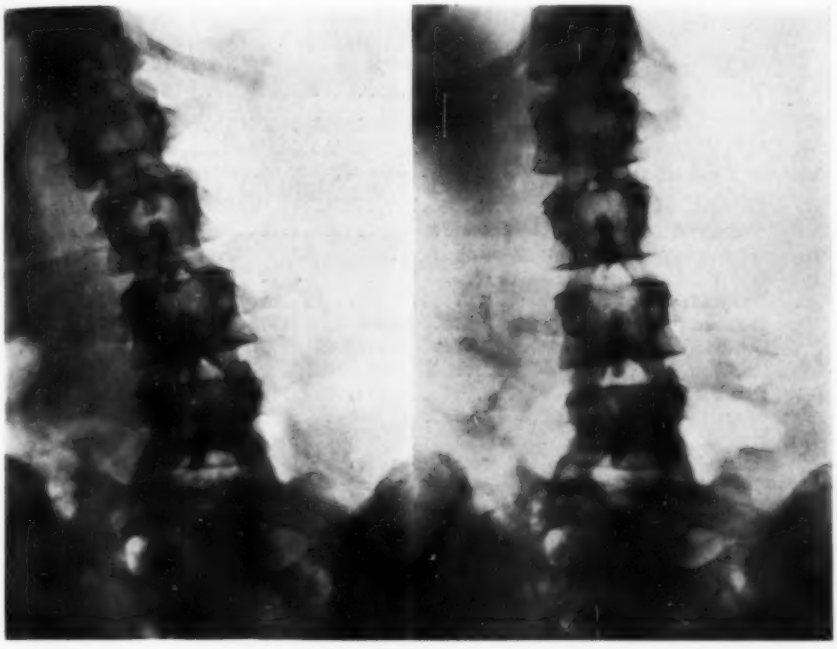

Fig. 1. Bilateral sacralization with left-sided nearthrosis. Normal bending to the right side.

Fig. 2. The same case under bending to the same side as the nearthrosis. A state of parallelism is seen in the second intervertebral space. The third and fourth intervertebral spaces are the centres of paradoxical angulation.

osteophytes and retracted anterior margins; "instability" was seen only in two cases. We have discussed the importance of these symptoms elsewhere (7); changed mobility associated with either narrowing or instability of the disks must be regarded as evidence of degenerative processes in the disks; the other findings establish the diagnosis in the presence of two of these three latter criteria.

Clinical Observations. It will be seen from table 2 that the ages of the patients ranged from 23 to 65 years, and that the duration of symptoms was in most cases less than two years. Two thirds of the patients with sacralization were within the fourth and fifth decades of life. The situation of the pain did not give any definite clue as to the nature of the affection. Physical examination did not reveal any diagnostic signs except for the reduced lumbar lordosis and the changed character of

Table 1

Roentgenographic findings

	Sacralization	Lumbarization
Bilateral	18	7
Right-sided	6	1
Left-sided	6	2
Total number of cases	30	10
Changed angulation	28	10
Narrowed intervertebral spaces	15	9
'Instability' (more than 2 mm)	—	2
Localized osteophytes	1	4
Marginal sclerosis	2	5
Retracted anterior margins	—	3
Schmorl's nodules	—	—
Scoliosis	2	—
Spina bifida	3	—
'Vacuum phenomenon'	—	—
Nearthroses	14	3
Arthroses of intervertebral joints	4	2

Table 2

Clinical findings

	Sacralization	Lumbarization
Men	6	1
Women	24	9
Total number of cases	30	10
Range of ages, in years	23–65	27–57
Duration of symptoms:		
Up to two years	18	10
More than two years	12	—
Symptoms:		
Low back pain	14	2
Low back pain with sciatic radiation	11	8
Sciatic pain only	5	—
Paresthesias	2	2
Signs:		
Reduced lumbar lordosis	5	10
Scoliosis	2	—
Changed lateral bending:		
On same side	2	5
On opposite side	1	5
Bilateral	8	—
Changed forward and backward bending	8	10
Direct and indirect tenderness	2	—
Atrophy of lower extremities	1	—
Paresis of lower extremities	2	1
Reflex changes	4	3
Hypesthesias	4	3
Myoses (*i. e.* localized 'fibrositis') only	20	8

the forward and backward bending of the spine in the presence of lumbarization.

In two patients with *sacralization* and three with *lumbarization* reflex changes and sensory disturbances were noted, for which reason these cases were interpreted as cases of prolapse of a lumbar intervertebral disk. However, this diagnosis was not verified by myelography or operation, because the symptoms disappeared after rest in bed and physiotherapy.

Clinically, there was thus no possibility of differentiating these cases from others with the syndrome of low back pain with sciatic radiation.

Discussion

In our opinion, sacralization and lumbarization can only be diagnosed roentgenographically, since the clinical findings and past history are of limited diagnostic value.

Compression of the nerves passing through the intervertebral foramina, arthroses of the intervertebral joints or nearthroses have been supposed to excite pain in sacralization. In concurrence with the observations of De Sèze, our investigations suggest that degeneration of the disks is, in many cases, a contributory factor in the production of symptoms.

In nine of the ten cases of lumbarization, roentgenographic signs of degeneration of the disks were present, for which reason degenerative processes must be assumed to be the principal factor in the excitation of pain.

Treatment. The treatment of patients with low back pain with sciatic radiation due to sacralization or lumbarization must aim at stabilization of the spinal column; it may be either conservative (rest in bed, a supportive brace) or operative (spondylodesis). In our cases conservative therapy was employed with good results.

SUMMARY

Roentgenographic studies of 30 cases of sacralization and 10 cases of lumbarization are reported and the clinical observations briefly mentioned. In most cases of lumbarization a roentgen examination of the spinal function will reveal signs of degeneration of the intervertebral disks. In the presence of sacralization, degenerative changes of the disks are found in some, and changes in the statical conditions in nearly all, cases.

ZUSAMMENFASSUNG

Röntgenologische Studien an 30 Fällen mit Sakralisation und an 10 Fällen mit Lumbarisation werden berichtet und die klinischen Befunde kurz erwähnt. In den meisten Fällen mit Lumbarisation wird eine röntgenologische Untersuchung der Wirbelsäulen-

funktion Anzeichen von Zwischenwirbelscheibendegeneration aufzeigen. Liegt eine Sakralisation vor, findet man in einigen Fällen degenerative Veränderungen der Wirbelscheiben sowie in nahezu allen Fällen Veränderungen der statischen Verhältnisse.

RÉSUMÉ

Etude radiologique de 30 cas de sacralisation et de 10 cas de lombalisation avec résumé des observations cliniques. Dans la plupart des cas de lombalisation l'examen radiologique fonctionnel du rachis montre des signes de dégénérescence des disques intervertébraux. Quand il y a sacralisation on trouve une dégénérescence discale dans certains cas et des modifications de la statique dans presque tous les cas.

REFERENCES

1. Brailsford, J. F.: Deformities of the lumbosacral region of the spine. Brit. J. Surg. 16 (1929), 562.
2. Ferguson, A. B.: The clinical and roentgenographic interpretation of lumbosacral anomalies. Radiology 22 (1934), 548.
3. George, A. W.: The vertebrae roentgenologically considered. W. Saunders. New York 1919.
4. Ghormley, R. K.: Symposium on backache in medical practice. Proc. Staff Meet. Mayo Clin. 26 (1951), 457.
5. Hasner, E., et al.: Roentgenological examination of the function of the lumbar spine. Acta radiol. 37 (1952), 141.
6. — Radiologisk-fysiurgisk undersogelse af lænderygsojlens funktion ved lumbago-ischias syndromet. (Danish.) Nord. med. 47 (1952), 516.
7. — Degeneration of lumbar intervertebral disks. Am. J. Phys. Med. 31 (1952), in print.
8. Hodges, F. J., and Peck, W. S.: Clinical and roentgenological study of low back pain with sciatic radiation. Am. J. Roentgenol. 37 (1937), 461.
9. Ingebrigtsen, R.: Sakralisation des fünften Lumbalwirbels. Acta chir. Scandinav. 65 (1929), 283.
10. Lindblom, K.: Technique and results of diagnostic disc puncture. Acta orthop. Scandinav. 22 (1951), 315.
11. Mitchell, G. A.: The significance of lumbosacral transitional vertebrae. Brit. J. Surg. 24 (1936), 147.
12. Reisner, A.: Kreuzschmerzen und lumbosakrale Übergangswirbel. Fortsch. Röntgenstr. 48 (1933), 31.
13. de Sèze, S., et al.: Transitional anomalies of the lumbosacral joint. Semaine d'hôp. Paris 27 (1951), 661.
14. Simons, B.: Röntgendiagnostik der Wirbelsäule. G. Fischer, Jena 1951.
15. Todd, T. W.: Numerical significance in thoracicolumbar vetrebrae of the mammalia. Anat. Rec. 24 (1927), 261.
16. Willis, T. A.: The lumbosacral vertebral column in man, its stability of form and function. Am. J. Anat. 32 (1923—24), 95.

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AN IMPROVED IRIDIUM-192 TELETHERAPY UNIT

By

H. F. Freundlich[1] and *J. L. Haybittle*

Introduction

In 1949 when large sources of cobalt-60 were not available in Great Britain, iridium-192 presented itself as a possible alternative for the production of a multicurie γ-ray source. The neutron capture cross-section of the target material, iridium-191 (388 barns) meant that high specific activities could be obtained after only a few months irradiation, and the mean energy of the γ-rays from iridium-192 (400 kev) was such that, while being high enough to minimize differential energy absorption in bone and soft tissue, adequate shielding could be provided in a simple, compact and cheaply constructed head. An iridium-192 teletherapy unit was therefore designed, and built, and has been in continuous clinical use at Addenbrooke's Hospital, Cambridge, since May 1950. A full account of its design and construction has appeared elsewhere (4). The source consisted of 4.4 gm of iridium foil 0.1 mm thick made up in the form of four concentric cylinders each 1 cm high, the largest being 2 cm in diameter. To overcome the disadvantages of a half-life of only 74 days, two identical sources were used, one being irradiated in the pile at A. E. R. E., Harwell while the other was in use in the unit. Every four weeks the sources were interchanged and the output at the beginning of each four week period when the reactivated source was put in the head was about 16 r/min. at a source-skin distance of 8 cm (8.5 cm from the centre of the source). Its performance was thus similar to an 8 gm radium teletherapeutic unit.

In view of the ease of construction and cheapness of an iridium-192 unit, it seemed worthwhile to build an improved machine having a higher

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output and greater flexibility of field size and source-skin distance. Such a machine we felt could be of great use to smaller radiotherapeutic departments with limited financial resources, as well as providing experience that might be valuable when multicurie sources of other γ-ray emitters in the same energy range *e. g.* caesium-137 (3), should become available. This improved radio-iridium unit has now been completed, and an account of its design, construction and physical characteristics is given below.

Design and Construction

The source had to be designed to fulfill the following conditions:

(1) The maximum number of spaces in the A. E. R. E. pile that could be allotted permanently for the reactivations was six.

(2) Owing to the high neutron capture cross-section, of iridium, it was considered inadvisable to put more than 1.4 gm in each irradiation space for fear of reducing the neutron flux in neighbouring spaces. Also to avoid self-shielding, the iridium should be in the form of foil not greater than 0.1 mm in thickness.

(3) The physical dimensions of each part of the source had to be such as to fit into the pile irradiation containers *i. e.* 2.5 cm diameter $\times$ 6 cm long.

(4) It had to be possible to perform the interchanging of the sources by simple remote control equipment.

Within these conditions the first method of increasing the strength of the source over that of the original unit would be to make it of six pieces of iridium foil each weighing 1.4 gm. The total weight of foil, and hence the source strength, would thus be increased by a factor of 1.9. It was pointed out by Mr. R. S. Quick of this department that a further increase could be obtained by using eighteen pieces of iridium, 1.4 gm each, twelve being in use in the head at any one time, while the remaining six were being reactivated in the pile. The sequence for each set of six sources would be 8 weeks use followed by 4 weeks reactivation, and as a result the source strength would be improved by a further factor of about 1.3. The total strength of source to be expected would therefore be 2.5 times that of the first unit.

The final design of the source was arrived at with these considerations in view, and is shown in fig. 1. Strips of iridium foil are held in position on the sides of duralumin wedges by aluminium caps riveted to the ends of the wedges. Twelve of these sources are contained in a duralumin cylinder 3 cm in diameter and 3 cm long closed at one end permanently, and at the other by a removable screw cap. A boss projecting from the closed end is grooved so that it may be gripped by a suitable tool, and holes are drilled

in the container opposite the ends of the twelve wedges. The function of these holes will appear later when the loading and unloading procedure is described.

The construction of the head is shown in fig. 2. To make the head as small as possible, the shielding material used was uranium supplied by A.E.R.E., who cast and machined the two parts to our specification. A rotating cylinder carries the source and in the *off* position the source is surrounded by 4.5 cm of uranium (in all directions except towards the nozzle where it is 3.5 cm), a thickness estimated from previous calculations (4) to be sufficient to reduce the dose rate at the surface to about 0.05 r/hr. The main body of uranium is enclosed in a steel shell on top of which is welded a steel plate carrying the motor and turning mechanism. The inner cylinder is also held in a steel casing which is attached to a spindle that runs in two ball-races mounted on the steel plate. This spindle is driven by a 1/20th H.P. electric motor via a worm gear and a Geneva mechanism (5). The latter ensures that the cylinder is quite firmly located in the *on* or *off* position and operates as follows. When current is supplied to the motor it always rotates in the same direction, and the roller on the driving gear engaging in the slots of the wheel turns the cylinder from *off* to *on* in three steps. When in the *on* position a limit switch cuts the motor current, and although the motor itself tends to overrun, the cylinder is held in position by the locking drum of the driving gear fitting into the corresponding circular recess in the wheel. To switch off, the circuit is again made to the motor, and the rotation continues by another three steps until stopped by the other limit switch in the *off* position. Provision is made by means of a small knurled knob attached to the rear of the motor spindle to perform the whole operation by hand if the current fails. When the source is placed in the uranium cylinder it is held by two pins which are able to pass through two slots in the steel casing around the cylinder, but which after a small rotation of the container prevent it from

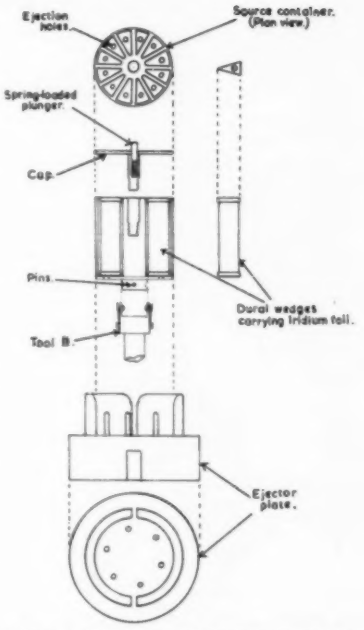

Fig. 1. Diagram of source-container and sources together with the end of the tool used for removing container from the head, and one of the ejector plates.

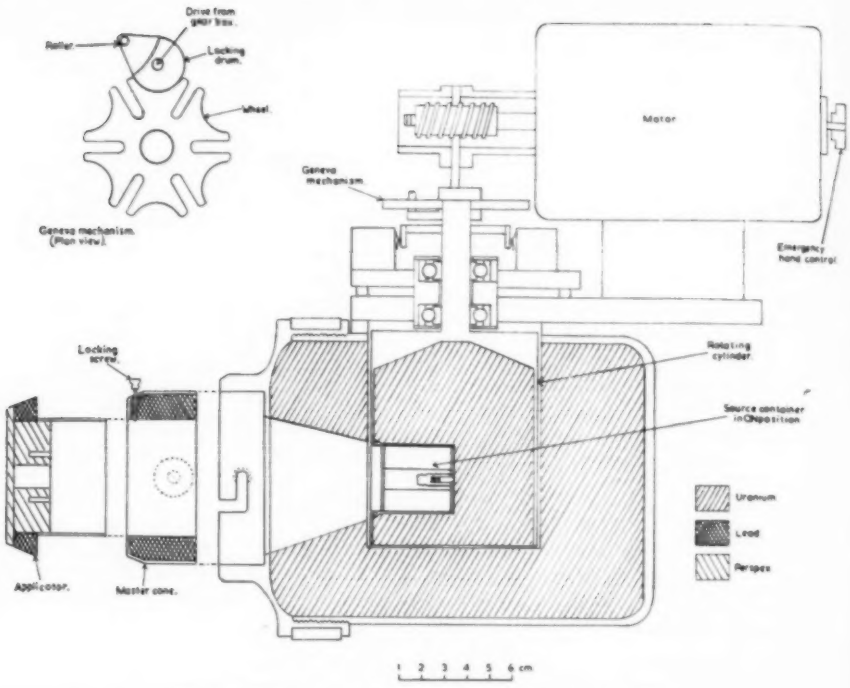

Fig. 2. Side-view of head and rotating mechanism.

falling out. A springloaded plunger in the cap presses the pins against the casing so that the container is firmly held in position.

It was decided that with the expected increase in output, facilities should be provided for using the machine at source-skin distances greater than 8 cm. The applicators are therefore designed to work at 9 cm and 13 cm source-skin distance, the longer distance giving improved depth-doses and also being more convenient to use on less accessible parts of a patient's body. A number of 'master cones' are used which fit into a bayonet fitting on the head. In fig. 2 a 'master cone' for use with fields up to 5 cm diameter and source-skin distance 9 cm is shown together with a 5 cm diam. circular applicator. The applicators are a push-fit into the cones and may be rotated to any desired angle, where they may be fixed in position by a locking screw. Lead diaphragms in the applicators define the field size, and the ends are covered with 1/8″ perspex to absorb any soft radiation scattered from the inner walls of the head. As will be seen later further perspex has to be added to the front face to flatten the isodose

curves. The largest fields obtainable are 7 cm and 9 cm diam. at 9 cm and 13 cm source-skin distance respectively.

A general view of the complete unit with the head pivoted in a steel stirrup and suspended from a standard Westinghouse type roentgen stand is shown in fig. 3. The beam directing device is a simple lamp and lens system producing a narrow beam of light coincident with the axis of the emerging γ-ray beam. It is mounted on a rotating ring fitted to the front of the head, and may be easily detached if not required as shown in the close-up view (fig. 4).

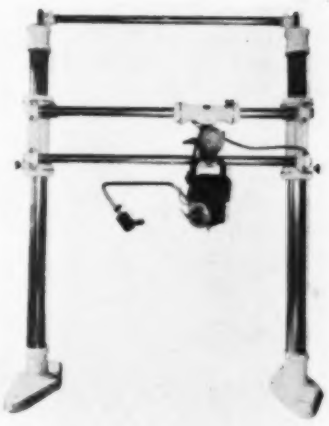

Fig. 3. General view of unit with beam director attached.

Loading and Unloading Procedure

The transfer of sources is done with the aid of the lead bench shown in figs. 5

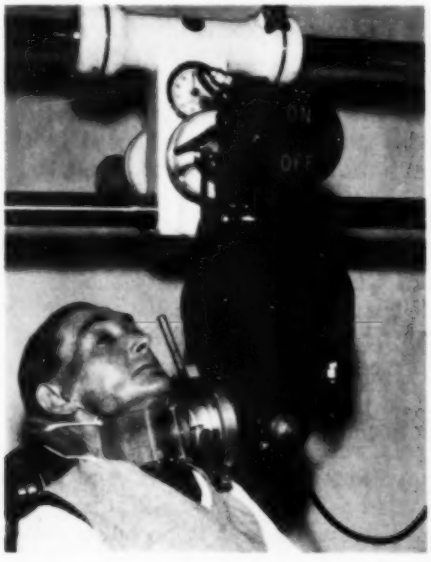

Fig. 4. Close-up view of unit being used for treatment of carcinoma of the larynx with a 3-field technique, the fields being positioned by means of the perspex former shown.

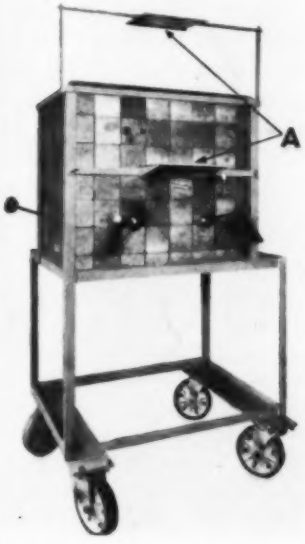

Fig. 5. Lead bench as seen from the operator's side.

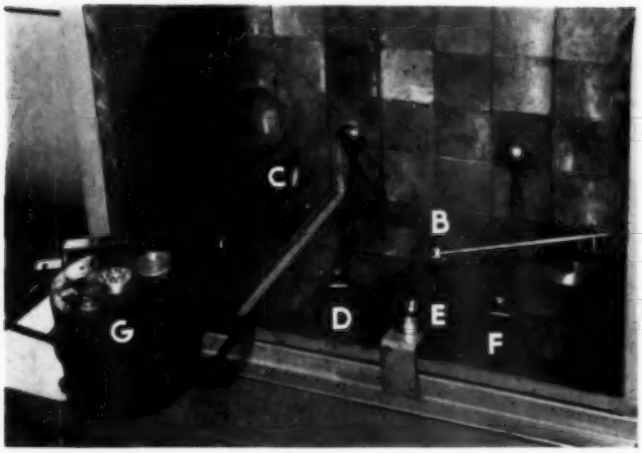

Fig. 6. Interior of lead bench showing tools and other equipment used for the change-over of sources.

and 6. This bench has 2″ thick lead walls and floor and completely shields the operator, who performs all the operations by means of remote handling tools similar to those described by RITCHIE and SPRAGG (6), viewing being obtained by the two mirrors A.

To change over the sources in the unit, the bench is wheeled into position so that the head points into it and towards the tool B. With the operator now behind the shielding the machine is switched to the *on* position. The tool B is pushed up the nozzle, and is able to grip the projecting boss on the source cylinder. A small rotation disengages the retaining pins, and the cylinder is withdrawn, and placed in the hole in the wooden block C. By pressing and turning anticlockwise the cap is unscrewed and left in the block, while the source cylinder is withdrawn, transferred to the tool D and placed on the ejector plate E. Six pins on this plate pass through the holes in the closed end of the cylinder and push up the six wedges that it is required to remove. (The next time the sources are changed a second plate is used which has pins so placed as to eject the other six wedges.) Tool F is then used to transfer the wedges one by one to the lead pot G. This pot contains a dural block having six holes drilled in it to take the sources, and when the lead lid is removed an internal spring pushes up the dural block so that it becomes accessible to the tools. A perspex cap protects the tops of the sources when they are in the pot. The reactivated sources when returned from A. E. R. E. are loaded into the unit by a reversal of the above procedure.

Each operation, loading and unloading, takes about ten to fifteen minutes. During this time film badges have been strapped to the front surface of the lead blocks, and the maximum dose recorded during any one operation has been 0.01 r. The risk to the operating personnel is thus negligible.

Physical Measurements

The radiation output was measured with a 100 r Victoreen chamber, placed in front of the applicator and the dose at the applicator surface estimated by application of the inverse square law. At the beginning of each four week period the dose-rate at 9 cm source-skin distance is about

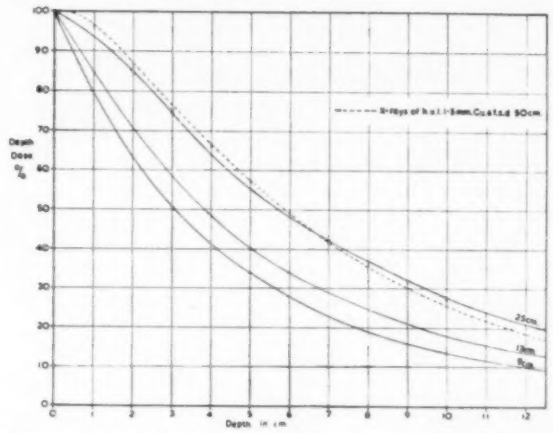

Fig. 7. Central axis depth dose curves for a 7 cm diameter field at source-skin distance of 9, 13 and 25 cm respectively.

23 r/min.[1] This is actually at a point 10.5 cm from the centre of the source. We therefore estimate that the source strength of the new unit is about 2.2 times that of the original machine. This is a little lower than had been expected. One possible explanation of the discrepancy is that the wedge-shaped sources are more self-shielding to the pile neutron flux than were the cylinders used in the first unit. Certainly the three sides of each wedge make up an effective cylinder of diameter about 4 mm, whereas the diameter of the smallest cylinder in the original unit was 11 mm. The output

[1] Since submitting this paper for publication, A. E. R. E. has made available to us a slightly higher neutron flux for the reactivation of the sources. As a result, the maximum dose-rates are now 27.5 r/min. and 14 r/min. at source-skin distances of 9 and 13 cm respectively.

with a 7 cm diam. circular field at 13 cm source-skin distance is about 11.5 r/min. at the beginning of each four week period.

Depth doses and isodose curves were measured in a water phantom (20 cm × 20 cm × 30 cm) using a small cylindrical perspex chamber of conventional design (Volume 0.16 cc. Wall thickness 2 mm) connected to a D.C. amplifier (1), the surface dose being estimated by half sinking the chamber in the front perspex wall of the phantom. In fig. 7 are plotted the central axis depth dose curves of a 7 cm diam. field at source-skin distances of 9 cm, 13 cm and 25 cm respectively. The latter is seen to compare favourably with that of roentgen rays of h. v. l. 1.5 mm Cu using a similar sized field and an f. s. d. of 50 cm, measured with the same apparatus. With the present unit the dose-rate at 25 cm is about 3 r/min. and is therefore too low for practical purposes, but if the source strength could be increased by a factor of 4 or 5 (see later discussion), this disadvantage would be overcome.

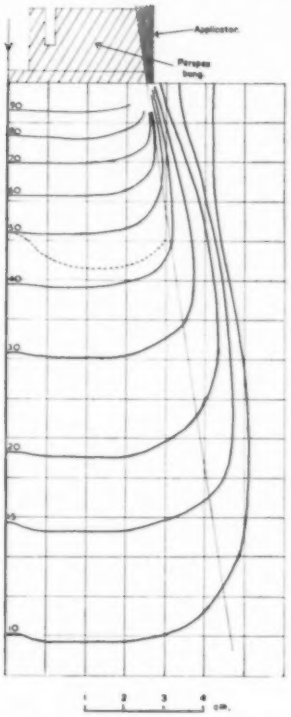

Fig. 8. Isodose curves for a field of 7 cm diameter at 13 cm source-skin distance.

As can be seen from the representative isodose curve shown in fig. 8 the penumbra outside the geometrical edge of the beam is well within tolerable limits. Owing to the arrangement of the iridium in the source the normal shape of these curves would be as indicated by the 50 % dotted contour. A perspex bung of the dimensions shown is fitted into the front of each applicator to produce the final isodose curves.

The unit is temporarily installed in a room originally built for a 220 kvp roentgen set, and the walls of the operator's cubicle are lined with 6 mm lead. It is so placed in the room that the head is always pointing away from the operator's desk and the neighbouring treatment room, and the maximum dose-rate it is possible to record at either of these places is of the order of 0.001 r/hr. In the direct beam the nearest wall is of brick and 3 metres away, and with no scattering material in the way of the beam the maximum dose recorded on the far side of this wall is 0.007 r/hr.

With the unit switched off, dental films (Ilford PM1) were strapped to various points of the head including the front surface of a 9 cm source-

skin distance applicator. The maximum dose-rate recorded by the films was 0.07 r/hr. in reasonable agreement with our predictions. A film placed at the nozzle with the applicator removed showed a dose-rate of 0.7 r/hr. These dose-rates are considered to be well within tolerable limits on the assumption that the operator's hands will never be in contact with the head for more than 5 hrs or in the nozzle region with applicator removed for more than half an hour during a working week.

Discussion

The unit described demonstrates the possiblities of using iridium-192 for teletherapy. The mean energy of its γ-rays falls in a most convenient region in that while being high enough to avoid the disadvantages associated with the selective absorption in bone of normal 220 kvp roentgen rays, it is still sufficiently low to make the amount of shielding required small as compared for example with cobalt-60. The resulting unit is therefore compact and cheaply constructed, and needs no heavy and complicated movable diaphragms for the control of field size. Against these advantages must be set the disadvantage of the short half-life of iridium-192, and the consequent need for frequent source changes and reactivation. The actual manipulation of the sources in making change-overs is a simple and safe operation using a similar procedure to that described above. Also boxes for transport of the sources need not be too unwieldy owing to the relative ease with which the γ-rays may be absorbed in lead.

There remains the problem of increasing output so that source-skin distances of 25 cm or more could be used. We feel that our present machine represents the limit of what may be achieved in Great Britain with the present limitations imposed by the pile at A. E. R. E. The maximum flux available is about 8×10^{11} neutrons/cm^2/sec. and the source strength is directly proportional to this figure. Other factors that influence the source strength are the number of spaces that may be used for reactivation, and the amount of iridium metal allowed per space. Where and when higher power piles are available for the production of isotopes for medical use *e. g.* at Chalk River and Arco (under construction) with fluxes of the order of 10^{13} neutrons/cm^2/sec. there should be no difficulty in constructing and operating an iridium-192 teletherapy unit having a larger output than the machine we have described.

Mention must be made finally of the possibilities of using caesium-137 in a teletherapy unit. As already pointed out by EASTWOOD (3) and BRUCER (2) this fission product combines the advantages of a long half-life with the emission of monochromatic γ-rays of relatively low energy (661 kev). Using the absorption data given by VICTOREEN (7), we have calcu-

lated that a caesium-137 unit with an output of 40 r/min. at a source-skin distance of 25 cm, would require 7.5 cm of uranium shielding to reduce the dose-rate at the surface of the head to 0.06 r/hr. Apart from this increase in shielding the general features of the design of such a machine could be similar to that we have described above. Unfortunately it is still doubtful when large sources of caesium-137 will become available owing to the difficulties associated with the chemical extraction of such high activities. RUPP (8) has estimated that it may be five years before large fission product sources will be available from Oak Ridge. In the interim period the possibilities of a wider use of iridium-192 seem worthy of consideration.

Acknowledgements

The authors are indebted to Mr. R. S. QUICK, now on leave of absence at the Strong Memorial Hospital, Rochester, N. Y., who was actively associated with the work in its initial stages, to members of A. E. R. E., Harwell for their helpful cooperation and for supplying the uranium parts, to Mr. A. BARKER and other members of the Cambridge University Engineering Laboratories who built the unit and played a large part in the design of its mechanical details, and finally to Professor J. S. MITCHELL for his continued help and encouragement.

SUMMARY

An improved iridium-192 teletherapeutic unit is described, having an output of 23 r/min. and 11.5 r/min. at source-skin distances of 9 cm and 13 cm respectively. Possibilities of further developments are discussed.

ZUSAMMENFASSUNG

Eine verbesserte Iridium-192 Teletherapie-einheit wird beschrieben. Sie hat eine Ausbeute von 23 r per Minute und 11.5 r per Minute bei einer Quellen-Hautdistanz von 9 cm bezw. 13 cm. Die Möglichkeiten der Weiterentwicklung werden diskutiert.

RÉSUMÉ

Description d'un appareil perfectionné de télécuriethérapie à l'iridium 192 débitant 23 r/min. et 11.5 r/min. à une distance focus-peau de 9 et 13 cm respectivement. Les possibilités d'améliorations ultérieures sont étudiées.

REFERENCES

1. ALLEN-WILLIAMS, D. J.: 'Thesis'. University of Cambridge. 1952.
2. BRUCER, M.: Some proposed teletherapy units. Nucleonics 10 (1952), 43.
3. EASTWOOD, W. S.: Possibilities of fission product cesium-137 for telecurie therapy. Nucleonics 10 (1952), 62.
4. FREUNDLICH, H. F., HAYBITTLE, J. L. and QUICK, R. S.: Radio-iridium teletherapy. Acta radiol. 34 (1950), 115.
5. LICHTWITZ, O.: Mechanisms for intermittent motion. Engineering 173 (1952), 452.

6. RITCHIE, A. B. and SPRAGG, W. T.: A set of parts for the remote handling of radioactive sources. J. Sci. Inst. 28 (1951), 214.
7. RUPP, A. F.: Problems in manufacture of fission product therapy sources. Nucleonics 10 (1952), 45.
8. VICTOREEN, J. A.: The calculation of X-ray mass absorption coefficients. J. Appl. Phys. 20 (1949), 1141.

FROM THE RADIUM CENTRE (DIRECTOR: PAUL JACOBY) AND THE DEPARTMENT OF PATHOLOGY (DIRECTOR: PROSECTOR JOHANNES VESTERDAL JØRGENSEN), THE COUNTY AND CITY HOSPITAL, ODENSE, DENMARK

EMBRYONAL LIPOSARCOMA

Report of a Case

by

Henning Skjoldborg

The great majority of fatty tumors are benign. Numerous publications on benign fatty tumors have appeared, whereas only a few reports on the malignant form are available, mainly because these latter are comparatively rare. A large statistical survey mentions only nine liposarcomas among 16,000 tumors of all kinds. The most peculiar feature of these rare tumors is their huge size. WELLS published a case in which a liposarcoma weighed 32 kg; tumors weighing between 20 and 30 kg were reported by WALDEYER and others, but the record is held by DELAMATER's patient, a woman with a retroperitoneal tumor, which protruded both from the perineum and the inguen, so that the circumference of the abdomen at the level of the tumor was 261 cm. About three years before her death, the patient weighed 117 kg, of which the tumor was estimated to constitute about 75 kg.

Lipomas are more common in women, but this sex distribution does not apply to liposarcomas. Of 173 previously recorded cases, 94 were found in men and 79 in women. The majority of these cases developed after the age of 40 and the average age of the patients was 53 years. On the other hand, cases in children of only two years of age have also been reported. Liposarcomas occur notably in the perirenal region, but they also show a predilection for the retroperitoneal tissue, the omentum and the mesentery. The growth rate, the development of metastases and the duration of the disease show great variation. Liposarcomas often run a very slow course, but may also lead to death within a short time, the extremes on record being 40 years and 4 months.

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However, the majority of cases are rather protracted with an average survival of several years. Metastases are comparatively rare, and in this connection it may be extremely difficult, in a given case, to decide whether it is a question of true metastases or only of multiple tumor formations (lipomatosis); in a few cases definite signs of malignancy have been observed in several such multiple lipomas, which have therefore been very difficult to evaluate. In some cases unquestionable metastases, occurring a long time after the removal of the primary tumor, have been observed. From the literature one gains the impression that metastases are less common than in other forms of malignant tumors; STOUT expressed the opinion that the frequency of metastases may be fixed at approximately 40 per cent. The majority of metastases are found in the lungs, pleurae, liver, bone marrow and central nervous system.

Macroscopically, the liposarcomas are most variable, but usually they form large, bulky, nodular masses of apparently well encapsulated tissue, which is firmer than the adipose tissue of simple lipomas; the colossal tumors are generally solid throughout with but a few softer degenerative areas. On rare occasions cystic areas may be observed. The color of the liposarcomas ranges from orange to pale cream, often with an admixture of red caused by necrotic or hemorrhagic areas; more than half are jelly-like. It is not uncommon for the tumors to contain areas of normal yellow fat interspersed among the more sarcomatous, partly fibrous masses.

Microscopically, the tumors show considerable variation, which may give rise to errors of diagnosis. Misdiagnoses were and, supposedly, still are not uncommon due to the rare occurrence of the tumors and the resulting lack of experience. SEIDELIN mentioned liposarcomas with cells resembling those of chordoma. MALLORY misdiagnosed a case in a man as metastases from a hypernephroma. Many cases of liposarcoma have primarily been diagnosed as myxomas, myxolipomas, etc.

The liposarcomas may be subdivided into four types (STOUT):

(1) The well-differentiated myxoid type resembling the usual type of embryonal fatty tissue. It consists of a capillary network with mature fat cells and embryonal stellate or spindle-shaped fat cells with droplets of a material, which stains with Scharlach R or Sudan III. The whole mass is bound together by a loose meshwork, which is generally, though not always, jelly-like. This characteristic picture is usually varied by the presence of more or less dense, fibrous connective tissue, with well-developed collagen and reticulin fibers. The lipoblasts, whether stellate or spindle-shaped, are comparatively small and of regular shape, and in spite of the enormous size of these tumors it is almost impossible to

Fig. 1. Retroperitoneal tumor measuring 14 × 16 × 18 cm. weight 6 kg.

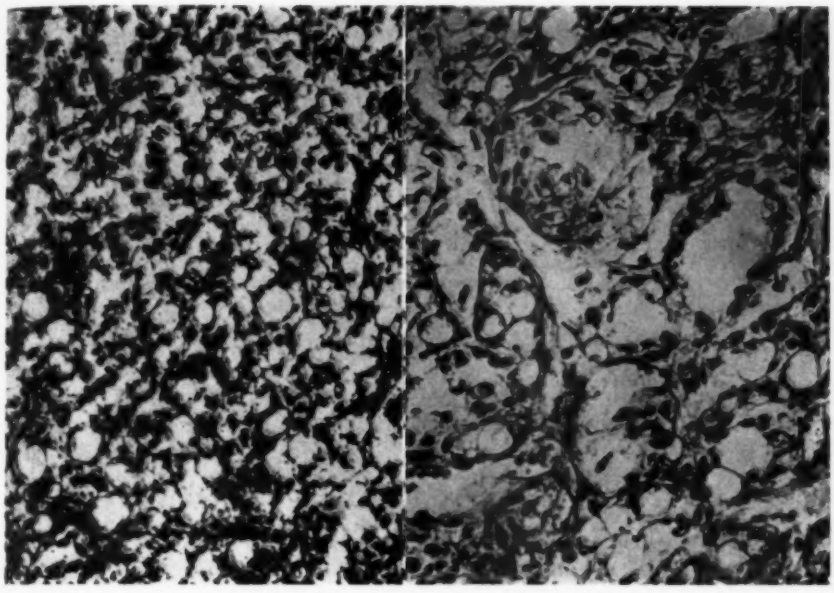
find any mitoses. Development of metastases seems to be extremely rare in this well-differentiated variety.

(2) The poorly differentiated type to some extent resembles the first type. The essential difference is that the lipoblasts are often bizarre and monstrous with astonishingly variable nuclear formations, and the nuclei are frequently hyperchromatic or pyknotic. These cells dominate the picture and the lipoid content is very sparse. Occasionally, signet-ring forms may be observed. Completely differentiated adipose tissue is practically absent, and the number and arrangement of the blood vessels are so variable as to be no longer significant. This poorly differentiated type is definitely malignant, difficult to eradicate, and may form metastases.

(3) In the round cell or adenoid type the characteristic lipoblast is a small rounded cell with a centrally placed nucleus and voluminous vacuolated cytoplasm; these vacuoles are filled with fat. The cells are massed together in a delicate fibrillar network with capillaries. In many such tumors the cells may attain an enormous size. Like the tumors of the second type, the round cell tumors are difficult to eradicate and may form metastases.

(4) Mixed types are composed of two or more elements of the preceding types and are, like these, malignant.

A feature common to all four types is that the tumors are markedly radiosensitive.



a. b.

Fig. 2. Histologic sections. Fat cells of all stages and development are dominating. a. × 50, b. × 125.

Case Report

Since the age of sixteen a 40-year-old man had had an indolent tumor behind the left malleolus. For two years before his first consultation the tumor had been developing slowly.

Otherwise the patient was completely well, and a general examination did not reveal any other anomalies. A diagnostic biopsy showed malignancy. After numerous misdiagnoses (metastases from a hypernephroma, synovial sarcoma, chordoma, myxoangioma, and lipoma) the diagnosis of embryonal liposarcoma was finally established.

Roentgen therapy was instituted before the final diagnosis was made, and resulted in a rapid disappearance of the primary tumor (2,040 r over three fields, 10 × 15 cm, 2 mm Al, 165 KV, 40 cm, 5 mA 2.4 min.).

Seven years later the patient developed complete flaccid paralysis. In the period which followed, tumors occurred in several situations. At first some benefit was derived from roentgen treatment, but the general condition of the patient slowly deteriorated, and death occurred nine years after his first consultation at the Radium Centre.

Autopsy showed an extremely emaciated man with numerous skin tumors. In the retroperitoneal tissue around the left adrenal gland there was a bulky, ill-defined tumor invading the surrounding loose connective and fatty tissues and, apparently, connected with some of the subcutaneous skin tumors. Its structure was fairly uniform, and the color varied from orange to pale cream via darker hemorrhagic areas to normal fat tissue,

interspersed with more sarcomatous masses with slightly soft, degenerative areas. The weight was 6 kg. Similar tumors were found subpleurally, in the lungs, in the ventricles of the heart in the form of gooseberry-sized polypous tumors, and in the body of the eleventh thoracic vertebra. On opening the spinal canal ingrowth through the intervertebral foramina was found. The parenchymatous organs were normal.

Microscopically, the tumor was composed of a reticular, fairly loose connective tissue. In many places it was jelly-like with a few more or less well-developed, fairly slender bundles of collagen fibrils; in other areas there was more immature reticular connective tissue. In this network many different cell forms were seen. One type of cells was very similar to reticulum cells, of which some were fibroblast-like. but the chief characteristic of the histologic picture was the great majority of fat cells, which were found in all stages of development. The most immature cells were small, fibroblast-like cells with bright cytoplasm containing one distinct vacuole or several small vacuoles and hyperchromatic or pyknotic, slightly eccentrically placed nuclei. All intermediate graduations between these immature cells and large, mature fat cells were present, and the latter variety did not look like tumor cells at all. Strikingly enough, mitoses were absent. Some peculiar, large, singly placed cells were observed here and there. Another feature, fairly characteristic of the tissue, was the large number of vessels with very thin walls, which were actually made up of endothelium alone. There were numerous larger and smaller hemorrhages into the tissue and several extensive necrotic areas.

Discussion

Surely, one of the most bizarre and fantastic chapters in the story of oncology (so STOUT says) is furnished by the tumors of fat forming cells. Many peculiar features and relationships and especially their astounding size make them of great interest.

The treatment of liposarcomas being dependent on microscopy, shows how important it is, here as in other cases, that the diagnosis of the nature of a tumor should be made with accuracy. Liposarcomas can be suspected clinically if they have reached a very large size, but the only proper procedure is biopsy, before treatment is instituted. The diagnosis of liposarcomas is not difficult because they have such distinctive histology that the only tumors with which they may be confused, are myxomas.

Differentiation is rather essential, as the myxoma does not form metastases, even though, not subjected to treatment, it keeps growing.

However, once having seen this tumor, it is fairly easy to recognize it, for, among other things, typical fat cells and lipoblasts are found.

The treatment of the well-differentiated type is first and above all surgical, as this type will rarely produce metastases. Concerning the other types, radiotherapy is the essential treatment before surgical therapy is attempted.

DESJARDINS in his great survey on radiotherapy gives the roentgen sensitivity of the various types of liposarcomas. An extraordinary high radiosensitivity is supposed to be characteristic of these tumors. The

less differentiated the tumor, the greater is the radiosensitivity. It is often possible to see the tumor diminishing from day to day as the treatment proceeds.

The embryonal liposarcoma mostly consists of immature fat cells, and the probable explanation of the marked radiosensitivity of the tumors lies in this fact, which other authors also have noted (EWING as early as 1935).

As a principle in the treatment of liposarcomas surgical therapy may be recommended. Failures are bound to occur, however, as in our case of a retroperitoneal tumor; such a situation makes complete removal impossible. In other cases the question is one of multiple tumor formations and in these, surgery cannot be employed.

It may not seem worth while to attempt extensive and severe operations in old and infirm subjects as the surgical risk may be greater than that inherent in the untoward results which may follow radiotherapy; this is especially so if the marked radiosensitivity of the tumors be taken into account.

It is not possible to establish rules to govern the treatment of every individual case; because the factors are so many and varied.

SUMMARY

The author reviews the literature on the subject and emphasizes the characteristics of embryonal liposarcoma. The various histologic types are described in detail. A new case is reported. The clinical and histologic appearance and the autopsy findings are described.

ZUSAMMENFASSUNG

Der Verf. gibt einen Überblick über die Literatur des embryonalen Lymphosarkomes und schildert das Charakteristische dieser Erkrankung. Die verschiedenen histologischen Typen werden eingehend beschrieben. Ein neuer Fall wird mitgeteilt; das klinische und histologische Aussehen sowie die Obduktionsbefunde werden beschrieben.

RÉSUMÉ

L'auteur passe en revue la littérature sur le liposarcome embryonnaire et en souligne les caractéristiques. Il décrit les différents types histologiques en détail. Il en présente un nouveau cas et décrit l'aspect clinique et histologique et les résultats d'autopsie.

REFERENCES

ADAIR, E. E., PACK, G. T., & FARRIOR, J. H.: Lipomas. Am. J. Cancer 16 (1932), 1104.
DELAMATER, J.: Mammoth tumor. Cleveland Med. Gaz. 1 (1859), 31.
DESJARDINS, A. U.: Radiotherapy. J. A. M. A. 105 (1935), 2065 and 2153.
EWING, J.: Fascial sarcoma and intermuscular myxoliposarcoma. Arch. Surg. 31 (1935), 507.

Fender, Fr. A.: Liposarcoma. Am. J. Path. 9 (1933), 909.
Hirsch, E. E., and Wells, H. G.: Retroperitoneal liposarcoma. Report of an unusually large specimen, with chemical analysis. Am. J. M. Sc. 159 (1920), 356.
Jacobi, A.: Congenital lipoma. Arch. Pediat. 51 (1934), 78.
Jaffé, R. H.: Recurrent lipomatous tumors of the groin. Arch. Path. 1 (1926), 381.
Mallory, F. B.: The Principles of Pathologic Histology. W. B. Saunders Co., Philadelphia 1929.
Moreland, R. B., and McNamarra: Liposarcoma, Arch. Surg. 45 (1942), 164.
Stout, S. P.: Liposarcoma — the malignant tumor of lipoblasts. Ann. Surg. 119 (1944), 86.
Wells, H. G.: Adipose tissue, a neglected subject. J. A. M. A. 114 (1940), 2284.

FROM DET NORSKE RADIUMHOSPITAL (DIRECTOR: DR. AXEL SCHEEL), OSLO, NORWAY

SOME PROGNOSTIC FACTORS, PARTICULARLY BIOPSY, IN CARCINOMA OF THE BREAST

by

Axel Scheel

The importance of early treatment of malignant tumours is stressed by all authors. Delay in treatment will affect the prognosis in a varying degree depending on the type of tumour. In cases of carcinoma of the breast great weight is attached to treatment being instituted as rapidly as possible. One often gains the impression that steps are taken hurriedly, more weight being laid on the factor of immediate treatment than accurate diagnosis, and possibly on the quality of treatment proposed. It is not so rare for biopsy to be omitted before radical operation in cases in which there is little opportunity of obtaining frozen sections. Many investigators are still of the opinion that excision biopsy augments the tendency to metastases per se, and the majority of authors emphasize the risk involved in any delay in radical operation following this procedure. There seems to be a consensus of opinion between authors who employ post-operative irradiation, that it is of the greatest importance that this be instituted as soon as possible after operation. In this respect it may happen that more weight is attached to the immediacy of the post-operative irradiation than to the quality of such treatment, the standard of which may leave much to be desired.

The author has attempted to assess the factors involved on the basis of a material of 300 consecutive operation cases (*Stages I & II*) at Radiumhospitalet during the period from the latter part of 1943 to the end of 1945. These have all been observed over a period of five years. Cases of death from intercurrent diseases have not been included.

The significance of the time interval between the first signs and radical operation has been dealt with by KAAE (1947). He shows clearly

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how the number of inoperable cases and the proportion between *Stage II and Stage I* grows larger with an increasing interval, which indeed one might expect. The material dealt with here is less suitable than that of KAAE for the elucidation of this relationship, primarily because it consists of operable cases only, and secondly because the writer has not had, as KAAE, the opportunity of examining personally more than a minimal number of patients. On the other hand the 5-year observation period to a certain extent affords an opportunity of directly evaluating the prognosis.

Table 1

History	Stage I	Stage II	Sign-free 5 years	Recurrence
Less than 6 weeks	66	44	80	30
(110 cases).....	(60 %)	(40 %)	(73 %)	(27 %)
6—16 weeks	49	28	58	19
(77 cases)				
More than 16 weeks	56	47	65	38
(103 cases)	(54 %)	(46 %)	(63 %)	(37 %)
Radical operation with no interval after first signs..	15 (abt. 60 %)	9 (abt. 40 %)	18 (abt. 75 %)	6 (abt. 25 %)

With the above reservations, a study of the material discloses that the prognosis becomes slightly though gradually worse in these operable cases. This fact is no doubt due partly to the fact that the most rapidly growing forms of growth are represented in the present material to a less degree than in that of KAAE. It appears clear, however, that there is no reason for precipitate action when a carcinoma of the breast has been diagnosed.

In this series more weight has been attached to the significance of excision biopsy. Neither cases of frozen section biopsy performed immediately before operation nor trephine biopsy have been included. There seems to be agreement among the majority of investigators that excision biopsy per se does not increase the risk of metastases, but some denounce it (for example ADAIR, HARRINGTON and GREENOUGH). In this paper the biopsy material in the two first stages has been dealt with separately and registered according to the histologic findings after operation. NOHRMANN (1949) has stated that this should not be done, as many of the cases may have passed from stage I to stage II in the course of the period elapsing between biopsy and radical operation (as a rule only a limited number of days). It is my impression that this will occur only to a very small extent in such a brief interval, as indicated by the previous table as well as by Table 3.

Table 2

Stage I (174 cases)	
Excision biopsy performed in 84 cases	75 without recurrence
	1 with recurrence
	8 died from cancer
No excision biopsy performed in 90 cases	74 without recurrence
	3 with recurrence
	13 died from cancer
Stage II (126 cases)	
Excision biopsy performed in 28 cases	13 without recurrence
	3 with recurrence
	12 died from cancer
No excision biopsy performed in 98 cases	44 without recurrence
	8 with recurrence
	46 died from cancer

There are no signs of worsening of the prognosis when excision biopsy has been performed. The figures are slightly better in such cases than in the others, and this must be due to the fact that biopsy was carried out more often in the less advanced cases in which the prognosis is more favourable. However, in this respect the material does not appear to be selective to any great extent, biopsy having been performed frequently in cases of relatively large tumours, and omitted on several occasions in the presence of relatively small tumours.

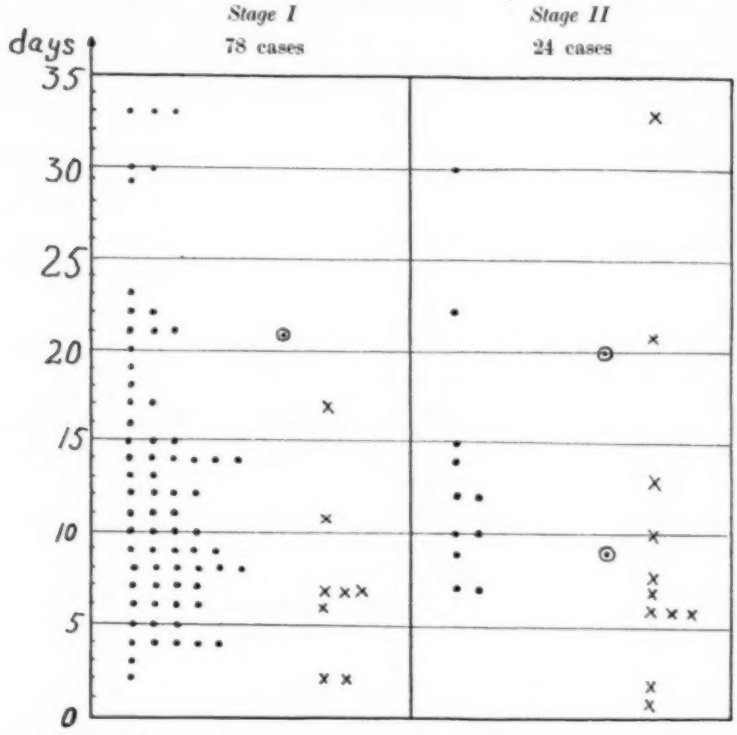
There seems to be general agreement that radical operation should be undertaken as soon as possible after a positive excision biopsy, and many investigators are of the opinion that delay, even for a few days, may be fatal. NOHRMANN et al. emphasizes this dictum which he has supported with statistics. His figures in the separate groups, however, are small.

From the present material I have arrived at a divergent conception of the position inasmuch as that there does not appear to be evidence that the prognosis is worsened when the interval between the excision biopsy and radical operation is increased from a few to more than thirty days. All 112 cases in which excision biopsy was performed, have been included in Table 3. Differentiation has been made between the two stages, but the relationship would have been identical if this had not been done. The figures are perhaps too small for a proper evaluation. The distribution of cases (cured, dead or with recurrences) suggest, however, the absence of risk with an excision biopsy, even if some weeks have passed before operation.

The figures which were available enabled a calculation of the average number of days between radical operation and postoperative irradiation to be made. It appears from Table 4 that taking the two stages separately the cases in which recurrence occurred later, show a somewhat longer

Table 3

The significance of time between excisional biopsy and radical operation stated in days. Cured: ●. Living with recurrence: ⊙. Dead of cancer: ×



No definite information of time elapsed: 10 cases.
Stage I: 6 cases cured; Stage II: 2 cases cured, 2 cases dead of cancer.

Table IV

Stage I	
Without recurrence 5 years (145 cases)	41.94 days average interval between radical operation and irradiation (+ 1 of 8 months and 1 of 5½ months)
Survived with recurrence and died later from cancer (25 cases)	44.32 days average interval between radical operation and irradiation
Stage II	
Without recurrence 5 years (58 cases)	49.12 days average interval between radical operation and irradiation
Survived with recurrence and death later from cancer (65 cases)	51.92 days average interval between radical operation and irradiation (+ 1 of 4½ months)

interval than those which remained free from recurrence after five years. The difference is very small, however, and is no more than about 5 per cent of the average number of days in both stages. Thus, it may be stated that irradiation should not be delayed unnecessarily long, although there appears to be no reason for a hurried commencement of postoperative irradiation.

Conclusions

The present material shows a gradual worsening of the prognosis as the interval between the first signs of carcinoma of the breast and radical operation increases. Broadly speaking, therefore, the development of the growth seems to be slow. The material is not entirely representative, however, for the evaluation of this correlation.

Neither the performance of excision biopsy nor the length of the interval between this and the subsequent radical operation can be observed to influence the prognosis. This latter point seems to be in conflict with current opinion.

The average number of days elapsing between radical operation and subsequent postoperative irradiation, lies slightly higher in the cases in which recurrence occurred later than in those which remained free from signs. The difference of about 5 per cent is small, however, and indicates that the length of the interval does not appear to play any large part in the prognosis.

SUMMARY

The study is based on a material of 300 consecutive cases of carcinoma of the breast operated upon at Radiumhospitalet, Oslo. The length of the interval between the first signs and the radical operation was found to have a smaller influence on the prognosis than expected. No effects due to the performance of biopsy or the length of the interval between this and the radical operation was observed. The patients who remained free from signs had received, on an average, post-operative irradiation slightly earlier after operation than those who had recurrences.

ZUSAMMENFASSUNG

Die Untersuchung stützt sich auf 300 fortlaufend registrierte Fälle von Brustkrebs, die im Radiumhospital in Oslo operiert worden sind. Man fand, dass die Länge des Intervalles zwischen dem ersten Krankheitszeichen und der Radikaloperation von geringerer Bedeutung für die Prognose war, als man es erwartete. Weder die Probeexzision noch die Dauer des Intervalles zwischen dieser und der Radikaloperation hatten einen erkennbaren Einfluss auf die Prognose. Die Patienten, welche symptomfrei bleiben, hatten im Durchschnitt die postoperative Bestrahlung etwas früher nach der Operation erhalten als die, welche Rezidive bekamen.

RÉSUMÉ

Ce travail est basé sur l'étude de 300 cas consécutifs de cancer du sein opérés au Radiumhospitalet d'Oslo. La durée de l'intervalle entre les premiers signes et l'opération

radicale a eu moins d'influence sur le pronostic qu'on ne s'y attendait. On n'a pas remarqué d'influence due à la pratique d'une biopsie ni à la durée de l'intervalle entre celle-ci et l'opération radicale. Les malades qui sont restées apparemment guéries ont subi, en moyenne, un traitement roentgenthérapique post-opératoire un peu plus tôt après l'opération que celles qui eurent des récidives.

REFERENCES

ADAIR, F.: The effect of preoperative irradiation in primary operable cancer of the breast. Am. J. Roentgenol. 35 (1936), 359.
— Rôle of surgery and irradiation in cancer of the breast. J. A. M. A. 121 (1943), 553.
GREENOUGH, R. B.: Early diagnosis of cancer of the breast. Ann. Surg. 102 (1935), 233.
HARRINGTON, S.: Carcinoma of the breast. Surg., Gynec. & Obst. 56 (1933), 438.
— Unilateral carcinoma of the breast treated by operation and radiation. Surg., Gynec. & Obst. 60 (1935), 499.
— Survival rates of radical mastectomy for unilateral and bilateral carcinoma of the breast. Surgery 19 (1946), 154.
KAAE, S.: Preoperative roentgen treatment in breast cancer. Acta radiol. 28 (1947), 153.
NOHRMAN, B.: Cancer of the breast. Acta radiol. Suppl. LXXVII (1949).

FROM THE CENTRAL INSTITUTE OF RADIOTHERAPY (DIRECTOR: PROFESSOR S. MUSTAKALLIO), HELSINKI, FINLAND

SMOKING AND PULMONARY CARCINOMA

by

Marja Koulumies

The increased incidence of pulmonary carcinoma registered in the last few years has aroused interest in the possible factors affecting its genesis. Intensive studies have also been made of the possible rôle of smoking on cancer of the lung.

As early as the end of the nineteenth century SOEMMERING suspected smoking to be associated with pulmonary carcinoma. At the turn of the century BROSCH, obviously the first, succeeded in producing experimentally malignant proliferation on the skin of guinea-pigs by smearing it with 'tobacco-juice'. Later too the cancer-producing quality of tobacco tar has been investigated by means of experiments. Its relationship to cancer growths of the respiratory tract has been investigated also in Finland, according to a personal communication from ERMALA-HOLSTI-SETÄLÄ, and phantoms as well as animal tests have indicated that the absorption of tobacco tar and its accumulation in the respiratory tract is most pronounced in the regions where cancer growths are generally situated in man.

What the cancer-producing agent in tobacco actually is still awaits solution. Besides tobacco tar, arsenic among other substances (DOLL and HILL) has been suspected as a contributory factor. Arsenic is used for dusting the seedlings of the tobacco plant to expel pests. Investigations made by the KENNAWAY group prove, however, that even extensive statistics fail to support the hypothesis that tobacco treated with arsenic-containing preparations is more conducive to cancer than tobacco free from any contact with arsenic.

S. MUSTAKALLIO ascertained in 1944 that patients with cancer of the throat were almost without exception smokers, and that they had started

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to smoke at a considerably younger age than the patients of the comparative material not suffering from cancer of the respiratory tract. — Statistics published during the last few years in different countries on the smoking habits of patients suffering from pulmonary carcinoma or cancer of the respiratory tract generally indicate with increasing clearness an association with the smoking habit. Thus, for instance, of the 684 pulmonary carcinoma patients of the Americans, WYNDER and GRAHAM, only 2 per cent were non-smokers or light smokers and 96 per cent had smoked for over 20 years. The number of women among patients with pulmonary cancer has been found small everywhere, being only about 10—20 per cent. This has been ascribed to the fact that they smoke less.

As it is of interest to know how Finland compares in this respect the writer has made the following investigation.

The material covers 351 cancer patients examined over the course of 16 years at the Central Institute of Radiotherapy of the University of Helsinki. The diagnosis was verified histologically and the patients were questioned at the time of taking their case histories about their smoking habit. Furthermore, the writer has placed 494 patients examined during the same period at the Central Institute of Radiotherapy in a special group. In these cases there was no biopsy verification of the diagnosis, but, judged from the clinical picture, roentgen examination, bronchoscopy finding (not infrequently) or operation, the condition was one of pulmonary carcinoma.

The control material has been collected by the writer from the Medical Out-Patient Department. Data on the smoking habit was obtained in 300 male patients of the same age living in similar circumstances. The inquiry was made, without selection, of every man over 40 years of age who attended the Department, from February 1 to March 14, 1952, and in whom there was no reason to suspect cancer. As a matter of curiosity the writer also chose 15 women over 30 years of age and not suffering from cancer as control material from the same hospital. None of the women smoked and had the writer continued the inquiry only the 24th woman would have been found to have been a smoker.

Results of the Writer's Investigations

The material covers only 15 women in whom the diagnosis is confirmed by biopsy; 2 are smokers. The figure for non-smokers among the 18 cases without biopsy verification is also 2. With such a small material of women no definite conclusions can be drawn and the study will consequently be restricted to men only.

Among 336 men with pulmonary carcinoma and in whom the diagnosis was verified histologically, smokers account for 99.7 per cent (*i. e.* there

Table I

Distribution of the material by sex and average age at start of investigation

	No. of cases	Per cent	Average age, years
Ca. pulm. Biopsy +			
Male	336	95.7	55.7
Female	15	4.3	49.9
Total	351	100.0	55.5
Ca. pulm. No biopsy			
Male	476	96.4	58.3
Female	18	3.6	57.0
Total	494	100.0	58.2
No cancer			
Male	300	95.2	56.2
Female	15	4.8	51.5
Total	315	100.0	55.9

was but one non-smoker). The ratio is approximately the same, or 99.2 per cent, in 476 cases without histologic verification. Of the 300 cases of the control material, smokers total 82 per cent (hence, 54 men are non-smokers).

Table II

Age at which men started smoking

	0—10 years		11—15 years		16—20 years		21—30 years		31 years	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
1. Ca. pulm. Biopsy + ... Cases 301	53	17.6	86	28.6	133	44.2	27	9.0	2	0.6
2. Ca. pulm. No biopsy ..... Cases 376	90	23.9	113	30.1	134	35.6	33	8.8	6	1.6
3. No cancer ..... Cases 246	16	6.5	52	21.1	103	41.9	67	27.2	8	3.3

$1 \longleftrightarrow 2^1$ $\chi^2 = 1.60$, $f = 3$, $P \approx 65$ Per cent

$1 \longleftrightarrow 3$ $\chi^2 = 47.3$, $f = 3$, $P < 0.1$ Per cent

$2 \longleftrightarrow 3$ $\chi^2 = 65.3$, $f = 3$, $P > 0.1$ Per cent

[1] $1 \longleftrightarrow 2$ comparison of groups 1 and 2
P = probability of the test hypothesis that the samples are drawn from the same population.

The average age at which the smoking habit started was 15.7 years for male smokers with pulmonary carcinoma confirmed by biopsy and 15.3 years for patients without biopsy verification. The figure is 18.8 years for male smokers of the control material. Patients with pulmonary carcinoma have consequently commenced to smoke earlier, many in childhood. A striking feature is the high number of boys who started smoking at the age of 10 years or younger. With them the potential cancer-producing elements in tobacco have had time in the course of the patient's life to irritate the mucous membranes of the respiratory tract over a longer period, and in childhood mucous membranes may be more sensitive to irritation. In patients with pulmonary carcinoma confirmed by biopsy, irritation due to smoking has continued before the verification of the disease for 39.7 years on an average (42.0 years in patients with no biopsy verification) and for 32.1 years in patients without pulmonary carcinoma. The duration of the irritation is thus 8—10 years longer for cancer patients than for those of the control material.

Table III

Type of smoking (men)

	No. of cases	Cigarettes; No.	Per cent	Pipe; No.	Per cent	Cigars; No.	Per cent
1. Ca. pulm. Biopsy + ...	279	274	98.2	5	1.8	—	—
2. Ca. pulm. No biopsy	361	351	97.2	10	2.8	—	—
3. No cancer	246	229	93.1	17	6.9	—	—

$1 \longleftrightarrow 2$ $\chi^2 = 0.16$, f = 1, P ≈ 70 Per cent
$1 \longleftrightarrow 3$ $\chi^2 = 8.53$, f = 1, P ≈ 0.5 Per cent
$2 \longleftrightarrow 3$ $\chi^2 = 5.90$, f = 1, P ≈ 1.5 Per cent

Cigar-smoking is rare in Finland at the social levels to which the patients of the material chiefly belong. Patients with pulmonary carcinoma are almost all cigarette-smokers. No difference has been found to exist between smokers of tipped and untipped cigarettes; all three groups contain an almost equal number of each.

Persons with pulmonary carcinoma have admitted, to a greater extent than the patients of the control material, to noticing that smoking causes irritation, the so-called smoker's cough. The percentage of patients with smoker's cough among 188 smokers with biopsy-verified pulmonary carcinoma is 87.2 (89.1 among 174 patients without a biopsy verification), whereas the figure is only 50 per cent for 246 smokers of the control material.

Table IV

Type of smoker (men)

	Heavy *a*)		Moderate *b*)		Light *c*)		Occasional	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
1. Ca pulm. Biopsy + ...	197	64.2	98	31.9	12	3.9	—	—
Cases 307								
2. Ca pulm. No biopsy	281	67.6	110	26.4	25	6.0	—	—
Cases 416								
3. No cancer	75	30.5	94	38.2	59	24.0	18	7.3
Cases 246								

a) One packet (20) or more of cigarettes per day.
b) $^1/_2$—1 packet of cigarettes per day.
c) Less than $^1/_2$ packet of cigarettes per day.

$1 \longleftrightarrow 2$ $\chi^2 = 0.90$, $f = 2$, $P \approx 65$ Per cent
$1 \longleftrightarrow 3$ $\chi^2 = 96.7$, $f = 2$, $P < 0.1$ Per cent
$2 \longleftrightarrow 3$ $\chi^2 = 110.6$, $f = 2$, $P < 0.1$ Per cent

Statistical treatment of the data has been carried out according to CRAMÉR. The results are identical for patients with pulmonary carcinoma with or without histological verification of the diagnosis, and the groups are also statistically equivalent.

SUMMARY

The investigation comprises 351 pulmonary carcinoma patients in whom the diagnosis was confirmed histologically and 494 patients with pulmonary carcinoma not verified by biopsy. The control material consists of 315 patients. The conclusions refer principally to men and the pulmonary carcinoma patients are almost all smokers who have smoked heavily for decades. In comparison with the control material, they have started smoking younger, often from childhood, and have smoked continuously for about 40 years, *i. e.* an average of 8—10 years longer than patients free from cancer. These circumstances are probably of significance in the genesis of pulmonary carcinoma.

ZUSAMMENFASSUNG

Die Untersuchung umfasst 351 Patienten mit Lungenkrebs mit histologisch bestätigter Diagnose und 494 Patienten, bei denen die pathologisch-anatomische Verifikation fehlt. Das Vergleichsmaterial besteht aus 315 Patienten. Die Schlussfolgerungen beziehen sich hauptsächlich auf Männer: die Lungenkrebspatienten waren fast alle seit Jahrzehnten starke Raucher. Im Vergleich zum Kontrollmaterial haben sie frühzeitiger zu rauchen angefangen, oft schon in der Kindheit. Sie haben regelmässig etwa 40 Jahre lang geraucht, im Durchschnitt etwa 8—10 Jahre länger als die Patienten ohne Lungenkrebs. Dieser Umstand ist wahrscheinlich für die Genese des Lungenkrebses bedeutungsvoll.

RÉSUMÉ

L'enquête porte sur 351 malades atteints de cancer du poumon confirmé histologiquement et 494 cas de cancer du poumon non vérifié par biopsie. Le groupe témoin comprend 315 sujets. Les conclusions concernent surtout des hommes et les malades atteints de cancer du poumon sont presque tous des fumeurs qui ont beaucoup fumé pendant des décades. Comparés au groupe témoin, ils ont commencé à fumer plus jeunes, souvent dès leur enfance, et ont fumé continuellement pendant environ 40 ans, c'est-à-dire en moyenne 8 à 10 ans de plus que les sujets indemnes de cancer. Ces faits sont probablement importants dans la genèse du cancer du poumon.

REFERENCES

Brosch, A.: Theoretische und experimentelle Untersuchungen zur Pathogenesis und Histogenesis der malignen Geschwülste. Virchows Arch. path. Anat. 162 (1900), 32.

Cramér, H.: Mathematical Methods of Statistics, p. 445. Almqvist & Wiksell, Uppsala 1945.

Daff, M. E. and Kennaway, E. L.: The Arsenic Content of Tobacco and Tobacco Smoke. Brit. J. Cancer 4 (1950), 173.

Doll, R. and Hill, A. B.: Smoking and Carcinoma of the Lung. Preliminary Report. Brit. M. J. 2 (1950), 739.

Ermala, P., Setälä, K. and Holsti, L. R.: Personal communication.

Kennaway, E. L. and Kennaway, N. M.: Studies of the Incidence of Cancer of the Lung and Larynx. Brit. J. Cancer 5 (1951), 153.

Mustakallio, S.: Über das Larynx- und Hypopharynxkarzinom, ihre Röntgenbehandlung und die Ergebnisse der Therapie. Acta radiol. 25 (1944), 13.

Wynder, E. L. and Graham, E. A.: Tobacco Smoking as a Possible Etiologic Factor in Bronchiogenic Carcinoma. A Study of 684 Proved Cases. J.A.M.A. 143 (1950), 329.

BOOK REVIEWS

URETHROGRAPHY IN THE MALE WITH A HIGHLY VISCOUS, WATER-SOLUBLE CONTRAST MEDIUM, UMBRADIL-VISCOUS U. By Olallo Morales and Ragnar Romanus. 104 pp., 88 illustrations, Acta radiol. Suppl. 95, Stockholm 1952. Sw. Kr. 20: —.

Up to now the main purpose of the roentgen examination of the male urethra has been to study gross alterations in the contours of the bladder and urethra; in some quarters it has also served as a basis for the study of functional disturbances in connection with micturition examinations. The new technique described, however, enables the roentgenologist to provide the urologist with more detailed information and the roentgen examination can thus compete with endoscopy in showing the finer details of the mucous membrane. It may also be used for studies of the functions of the motility of the urethra and the adnexal glands. Furthermore, it has a great advantage over endoscopy in that the roentgenograms may be preserved and re-examined at will, thereby providing a permanent record of development.

These detailed investigations, however, demand separate examinations of the bladder and urethra. A contrast medium suitable for the bladder examination is too dilute for use in the urethra; at the same time, too strong a contrast density in the urethra will often obscure finer details in the mucous membrane relief.

A complete urethrographic examination of the male urethra should, therefore, include: a) films exposed during injection with the lumen fully distended in order to demonstrate strictures, deformities and displacements of the lumen, and b) films taken during compression or evacuation. Evacuation films of the anterior urethra may be obtained by allowing the contrast medium to flow out passively (owing to the elasticity of the urethral walls), leaving only a thin layer covering the mucous membrane; compression films of the posterior urethra are best obtained by instructing the patient to contract the pelvic floor (with the external sphincter), thus pressing the contrast medium up into the bladder. These latter roentgenograms will show the finer mucous membrane alterations and, at the same time, the motility of the lower urinary organs and genital adnexae. The examination should, if possible, be completed with micturition films.

The urethrographic examination should include the vesical trigone and the posterior portion of the bladder floor as well as the whole urethra, since pathological conditions in the male accessory glands are often associated with changes in these regions. The rest of the bladder, on the other hand, belongs diagnostically and pathologically more with the upper urinary passages and is most suitably examined in the course of urography.

A number of the physical properties of fluids such as viscosity, surface tension, miscibility, wetting capacity, and film formation as well as some of the laws of hydrodynamics are discussed. These are of particular importance and value in understanding the course of micturition and the urethrographic examination.

It is evident hydrodynamically that 'bar formation' (constriction of the actual drainage opening of the bladder) presents a significant obstruction to micturition. The distance of a stricture from the bladder is, however, otherwise of no hydrodynamic importance.

The absence of prestenotic dilatation does not rule out the possibility that a stricture has already begun to affect the course of micturition.

The various pressure relationships in different parts of the urethra with low and high viscosity contrast media are discussed in relation to hydrodynamic laws and with the help of examples. The high rate of flow and low pressure obtained when a low viscosity agent is injected are in contrast to the low rate of flow and high pressure obtained with a preparation of high viscosity.

Any type of retrograde contrast medium should be able to produce satisfactory distention of the anterior urethra. To obtain adequate distention of the posterior urethra, however, a highly viscous agent is required.

A water-soluble preparation which wets and, due to high viscosity, adheres to the mucous membrane is necessary in order to show the mucosa in relief in evacuation films.

With consideration for the patient's comfort and to reduce the possibility of reflex muscle contraction due to irritation caused by the medium, mucous membrane anesthesia should always be used. The irritation is reduced, however, by the viscosity-increasing component.

Fluoroscopic control during the urethrographic examination enables the examiner to concentrate on actual regions to study the motility and reduces the danger of urethrocavernous reflux, which has a particularly low incidence with the high viscosity preparation.

This technique for urethrography is described in detail. The roentgenograms obtained are analysed.

If the contrast agent has a high contrast density, it contributes to the demonstration of the contrast filling of para-urethral ducts. In addition the material should be capable of wetting the mucous membrane and be miscible with the secretions in the ducts. High viscosity causes no interference. The pelvic floor contraction technique also facilitates the identification of contrast material located in para-urethral structures around the posterior urethra.

The authors compare the films obtained with the usual technique employing a low viscosity contrast medium with those in which the new technique and the highly viscous preparation, Umbradil-Viscous U was used. In general, comparisons between different methods and contrast media are based on the use of one method or one contrast medium as opposed to those used or published previously. The authors' comparison, however, is founded on a series of complete concurrent examinations of 83 cases, and thus provides a sound basis for evaluating both the methods and media. The result of the comparison has shown the new method to be superior to that used previously for diagnosis, admitting a more definite prognosis and more exact treatment in 60 % of all the cases, and giving valuable formation in every case examined.

The studies were originally intended to develop a special examination of the posterior urethra and which would serve as a supplement to a preceding examination with a low viscosity urography agent. It was discovered, however, that the new method was fully able to be substituted for the low viscosity method in examining the male urethra and bladder floor.

Urethrography of the male urethra is therefore best accomplished during fluoroscopy with a water-soluble, highly viscous preparation, containing a urographic contrast medium in relatively high concentration, a non-irritating viscosity-increasing substance and a rapidly acting anesthetic agent. The films are most satisfactorily made during injection, voluntary contraction of the pelvic floor immediately following discontinuation of the injection, and, if possible, during micturition.

Autoreview.

ROENTGEN EXAMINATIONS IN ACUTE ABDOMINAL DISEASES. By Johan Frimann-Dahl. 321 pages. 357 illustrations. Charles C. Thomas, Springfield, Ill., U. S. A., 1952. $ 10.50.

This book, now published in English, is an enlarged and modernised edition of the author's previous work (1939) in Norwegian. A synopsis in an international language on the roentgen diagnostics of acute abdominal conditions previously being practically non-existent, this book fills a real need; and it is a matter of satisfaction that the author.

who is probably the greatest of the authorities now active in this field, should impart his experiences in this form.

The work is lucidly arranged and aims at constituting a general survey of the subject although it also contains more detailed chapters, especially on the diagnostics of the ileus. In them, new conceptions based upon clinical observations and experimental investigations are provided. The author has not dealt with changes due to inflammation as exhaustively.

The style is easy flowing. The picture material is carefully chosen as well as abundant. A good many of the films, however, in spite of being in other respects of good quality, have deteriorated as a result of the considerable degree of reduction. Numerous schematic figures facilitate the reading matter.

It would be worthwhile and interesting if the author's great experiences were supported by statistics. It is to be expected that this book will be studied with the greatest consideration not only by radiologists, but by clinicians, especially surgeons. It is just these latter who naturally are interested in learning as to the degree in which roentgen examinations are successful in various spheres, the correctness (or incorrectness) of such examinations, and, if no direct diagnosis was made, the extent to which the examination formed a guide or basis for the subsequent procedures.

One of the signs of ascites described by Hellmer in 1942 and founded, as far as can be judged, on the erroneous interpretation of roentgen appearances, has been accepted by the author. Even the most meticulous technique of examination will fail to define the contour of the liver from ascitic fluid. A sign of this nature appears to me to demand either a mixing of chyle with the ascitic fluid or the superimposition of the greater omentum upon the liver area, of which there is a strong possibility in ascites. In the films which are intended to show this sign and in which the wall of the bowel also appears, it seems that the latter as well as the liver present markedly denser formations than the layer between them. Ordinary ascitic fluid would not have produced a phenomenon of this nature.

It is hoped that the work will become widely distributed both among the all too many who, as yet, have not participated in this important branch of roentgen diagnostics as well as among those who, being so engaged, are desirous of enriching their knowledge.

Hans-G. Skarby.

EINFÜHRUNG IN DIE ENZEPHALOGRAPHIE (PNEUMENZEPHALOGRAPHIE). Von Otto Schiersmann. 2. verb. Aufl. 135 Seiten, 186 Abb. Georg Thieme Verlag, Stuttgart 1952.

In the preface to this second edition we read: "as the type-settings and the blocks had become war casualities, a new edition became a necessity. This initiated a complete revision of the book. In carrying out such revision, great attention was paid to the more up-to-date methods as well as to more recent literature on the subject." Unfortunately, the author's efforts have not been crowned with success. No reference at all is made to the investigation of the posterior cranial fossa during insufflation. The author does not appear to know how a modern encephalography should be carried out so as to bring all the anatomic detail into view. It would seem that his technique must be unsatisfactory for otherwise he could not write: "in the lateral and horizontal views, a dilated third ventricle is well seen and which, if undilated, is hardly visible. If a good rendering of the third ventricle is obtained, one may assume that it is abnormally distended." His technique being what it is, little surprise is occasioned when he continues: "practically speaking, the differentiation between the normal and the abnormal by radiographic means, rarely succeeds. This will have to be decided from the history and the clinical findings if mistakes are to be avoided . . . In dealing with particular conditions, I shall have to explain that although certain radiographic findings may appear to be

normal in one case, they will have to be assessed as pathologic in other cases." With a conception such as this, encephalography ceases to be an objective method. It would be going too far if all the mistakes and imperfections of this work were to be enumerated. Be this enough to illustrate its value.

I. Wickbom.

SYMPOSIUM ON PHYSIOLOGICAL EFFECTS OF RADIATION AT THE CELLULAR LEVEL. Sponsored by the Biology Division, Oak Ridge National Laboratory. Reprinted from J. of Cellular and Comparative Physiology, Vol. 39, Suppl. 2, 1952.

This volume is the fourth in a series of publications from the Oak Ridge Laboratories on current problems in radiobiology. According to the general scheme of these conferences, part of the lectures are given by leading biologists and chemists for the purpose of presenting a broad and general survey of fields which may be of interest to research workers in radiobiology, *e. g.* physiology and biochemistry. Two of the lectures, delivered by DOUNCE and GREEN are accordingly devoted to enzyme chemistry and to the isolation of various cell components together with the effects of radiation on them.

The remaining seven lectures were by specialists within certain fields on the results of experimental investigations. The symposium does not give therefore a general outline of radiobiology.

V. SALLMANN has investigated the cytology of the irradiated eye and shows that fragmentation and clumping of chromatine as well as formation of vacuoles in the cytoplasm precede clinically visible changes by several weeks.

Alterations in the permeability of cell walls following upon irradiation are the subject of no less than three lectures by MC CUTCHEON, PARPART and SHEPPARD. Erythrocytes are especially studied and are known to be rather insensitive to radiation in contrast to the white blood cells, as far as visible histologic effects are concerned. SHEPPARD gives, however, evidence of a potassium leakage through the cell wa immediately after irradiation.

Nerve tissue is also known to be resistant to roentgen rays, but here, too, permeability changes in the axon seem to occur (NACHMANSOHN).

Two more articles deal with the effects of the atomic bomb irradiation on marine algae at Bikini (BLINKS) and the effects of irradiation on respiratory metabolism (BOELL).

The symposium stands on the same high level as the previous ones in these series. The four symposia together with those to appear in the future will give a modern outline of the genetic and physiologic effects of irradiation.

Arne Forssberg.